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ACROLEIN HEALTH EFFECTS

with Contributions by

Bonnie L. Carson

Cecily M. Beall
Harry V. Ellis III
Larry H. Baker
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FINAL TASK 6 REPORT
December 23, 1981

Contract No. 68-03-2928
Task Specification No. 6

"Health Effects Support for the Emission Control Technology Division"

For

Emission Control Technology Division
Office of Mobile Source Air Pollution Control
U.S. Environmental Protection Agency
2565 Plymouth Road
Ann Arbor, Michigan 48105

Attn: Robert J. Garbe

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16. ABSTRACT

Health effects literature primarily related to inhalation exposures to acrolein was collected, evaluated, tabulated, and summarized. Approximately 125 documents were collected from computerized and manual literature searches covering the period 1911-1981. Pharmacologists and an M.D. epidemiologist rated the documents according to their applicability to the study and their methodology. The approximately 45 documents considered useful for deriving a range of concern for human exposure to acrolein from automotive emissions were tabulated. The pages of tables detail the results of acute, repeated dose, and chronic testing of mice, hamsters, rats, guinea pigs, chickens, rabbits, cats, monkeys, dogs, and humans as well as human occupational and accidental studies. Most of the documents evaluated are described in an annotat-d bibliography.

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PREFACE

This report on health effects of acrolein was prepared by Midwest Research Institute (MRI) as Task No. 6 under Contract No. 68-03-2928, "Health Effects Support for the Emission Control Technology Division" for the U.S. Environmental Protection Agency.

Health effects literature primarily related to inhalation exposures to acrolein has been collected, evaluated, tabulated, and summarized so that this report can be used to derive a range of concern for human exposure to vehicular atmospheric emissions of acrolein.

Task activities were coordinated by the project leader, Mrs. Bonnie L. Carson, Senior Chemist, and the task leader, Ms. Cecily M. Beall, Assistant Scientist. Documents were rated and summarized by senior pharmacologists Drs. Harry V. Ellis III and Betty L. Herndon, of MRI, and epidemiologist Larry H. Baker, M.D., MRI consultant, who is Associate Professor of Community Health at the University of Kansas Medical Center. Data were tabulated by Ms. Beall, who, along with Mrs. Carson, contributed to the annotated bibliography. This study was performed under the general supervision of Dr. Edward W. Lawless, Head, Chemical Impact Assessment Section.

Mr. Robert J. Garbe was the project officer for the Emission Control Technology Division, U.S. Environmental Protection Agency, and Ms. Colleen DeMeyer served as Branch Technical Representative.

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SUMMARY

This summary of the health effects of inhalation of acrolein (CH_2=CH-CHO) is organized into the following sections: Goals and Methods, Bioassays, Animal Exposure Studies, Human Exposure Studies, and Recommended Range of Concern.

GOALS AND METHODS

The purpose of this compilation of data on acrolein inhalation exposures is to assist the Emission Control Technology Division (ECTD) of the U.S. Environmental Protection Agency (EPA) to establish the ranges of exposure conditions that are of concern for acrolein in exhausts from vehicles equipped with catalytic converters, and to be able to advise automobile manufacturers thereof. The situations of concern are during malfunctions and during exposures in traffic jams, parking and home garages, and other situations where little dilution of the exhaust is expected before inhalation. Most of the report is, as directed by ECTD, in the form of tables based on the literature reviewed. Data from exposures at levels higher than those of primary concern are included because strictly relevant information was scarce and these related data might prove helpful in assessing health effects at lower levels.

Documents on inhalation effects of acrolein identified from manual and computerized literature searches were rated in a two-step process by the project pharamacologist and epidemiologist. First, the document received an A, B, C, or D rating according to its applicability for deriving a range of concern for acrolein in automobile emissions. Second, if the paper was not a low-rated, foreign language document*, a theoretical paper, a review, or a nontoxicology experimental paper, it received a numerical score based on itemized features that should be present in an ideal report. For the most part, only A- and B-rated documents were tabulated; but when C- or D- rated studies involved low-level acrolein exposures, these were also tabulated. Blanks in the tables should be construed as denoting missing information in the documents.

BIOASSAY TESTS

In vitro studies show acrolein to be an inhibitor of ciliary activity and possibly a weak mutagen. Its possible carcinogenicity is also discussed.

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* Most foreign language articles rated C and D were usually not translated. Each foreign language document tentatively rated A or B from an English language abstract or brief examination of the paper was translated in sufficient degree to judge the experimental design and details. These papers were numerically scored from the translation.

In vitro tests on respiratory tissues: Only those tests using respiratory tissues and gaseous acrolein and reporting the acrolein levels used are tabulated in Section II. This tabulation has ignored the in vitro studies that evaluated the enzymatic changes brought about in animals by acrolein exposure, because they did not fulfill these criteria. Also, there is no adequate way to evaluate or extrapolate from the enzyme studies to an inhalation dose level for man. A thorough description and discussion of all types of in vitro studies is given in ECAO (1980).

Many of the tabulated (Table II-1) studies looked at irritant effects of acrolein, using tracheal cilia motion to quantitate acrolein dose-effects. The lowest level tested for effect on ciliary activity was 31.2 mg acrolein/m^3, causing ciliostasis in rabbit tracheal sections in ~ 36 min (Dalhamn and Rosengren, 1971).

Battista and Kensler (1970) interpreted their ciliary bioassay results as showing acrolein to be one of the most potent components of cigarette smoke. Macrophage function bioassays, however, specifically excluded acrolein as being a contributor to cigarette smoke toxicity (not tabulated: Haroz and Mattenberger-Kreber, 1977; Leffingwell and Low, 1979). However, Voisin et al. (1979, 1980) reported that ATP levels in macrophages decreased 20-70% following 30-min exposures to 18.6-81.6 mg acrolein/m^3.

Other bioassays: The mutagenic, carcinogenic, and teratogenic potential of acrolein has been thoroughly reviewed in ECAO (1980) and SRC (1979) (identical reviews).

Acrolein has shown "low," "borderline," or "moderate" mutagenicity depending on the test system and the author's frame of reference. No base-pair or frameshift mutations were found by two different groups using different test systems. Neither activated nor unactivated bacterial systems produced point mutations. Undescribed levels produced Drosophila mutations according to a 1945 report. One recent report described mutagenic changes (nucleic acid chain insertions/deletions) by acrolein when Salmonella typhimurium TA1538 and 98 were exposed (ECAO, 1980; SRC, 1979).

Two chronic whole-animal carcinogenicity studies using hamsters have been performed. The results of Feron and Kruysse (1977) have been summarized in Table III-4. In the study of exposure to 9.2 mg/m^3 for 7 h/d, 5 d/wk, for 52 wk, acrolein gave no indication of carcinogenic activity or co-carcinogenic activity with diethylnitrosamine, and had a minimal effect on the carcinogenic activity of benzo(α)pyrene (BP).

The unpublished results of a bioassay sponsored by the National Cancer Institute show no evidence that acrolein was a carcinogen or a co-carcinogen with BP or with ferric oxide (ECAO, 1980; SRC, 1979). The hamsters had been exposed to 11.5 mg acrolein/m^3 6 h/d, 5 d/wk, throughout their lifespan.

IARC (1979) concludes that the small amount of animal data and the lack of human data precludes an evaluation of the carcinogenicity of acrolein.

One study exposing male and female rats to 1.24-1.31 mg acrolein/m^3 for 26 d found no effect on the number of pregnant rats or the number and average weights of the fetuses (Bouley et al., 1975 and 1976) (see Table III-6). No longer-term studies have been done.

ANIMAL EXPOSURES

Acrolein is well known as an extremely irritating chemical, more potent than either its saturated analogue, acetaldehyde (CH_3CHO), or the prototype aldehyde, formaldehyde (HCHO) (see standard texts, such as Amdur, 1980). Upper respiratory tract retention of acrolein in dogs is ~ 80% (Egle, 1972), so that is the site of most of the irritation. Acrolein is a major toxic component of fires, and is the usually cited representative of the complex mixture of aldehydes and ketones which causes delayed deaths 6 to 72 h after "smoke inhalation." Much of the experimental data was inspired by this source, so most studies are of acute exposures. These studies are completely described in Section III, summarized by concentration in Table III-16, and summarized here in Table S-1.

Mouse studies: Most acute data (see Table III-1) are from the work of Kane and Alarie (1977, 1978), who studied acrolein alone and with formaldehyde. They found effects (decrease in respiratory rate) at the lowest levels tested (0.68 mg acrolein/m^3 or 0.28 mg acrolein/m^3 plus 0.46 mg HCHO/m^3). Repeated dose studies (Table III-2) showed similar results: some effects during a 10-min exposure to 1.03 mg/m^3 following acute exposures to 0.40 mg/m^3 in the previous days. There was some evidence of tolerance (at lower levels of 0.4 mg/m^3) and some of sensitization (at higher levels of 1.2 and 4.0 mg/m^3) from repeated dosing.

Hamsters: Feron and Kruysse (1977) and Feron et al. (1978) did 52-wk (12-mo) and 13-wk (3-mo) studies on hamsters exposed for 6 or 7 h/d, 5 d/wk (Table III-4). Exposure to 0.93 mg/m^3 produced no effects at all, while 3.3 mg/m^3 caused minimal effects: sleeping and restlessness during exposure, minimal inflammation in the nasal cavity. Higher doses were much more toxic, with a variety of effects. Histopathologic effects were found in the respiratory tract, basically as a reaction to inflammation.

Rat studies: The rat acute dose studies (Table III-5) were not very useful, the lowest level tested being 4.9 mg/m^3. However, there are several interesting repeated dose studies (Table III-6). Lyon et al. (1970) exposed rats continuously for 90 d. A concentration of 0.51 mg/m^3 had no effect, while 1.6 mg/m^3 caused pulmonary inflammation and occasional emphysema, 2.3 mg/m^3 affected weight gain, and higher doses caused various nonspecific inflammatory changes.

Bouley et al. (1975, 1976) did a variety of studies on specific pathogen free rats exposed to 1.24 to 1.31 mg/m^3 for various periods of time (Table III-7). These exposures were toxic (decreased body weight and food consumption), but effects decreased during exposure and recovery occurred afterward, in 39 d. There were no effects on reproduction. When challenged with an aerosol of pathogenic bacteria after exposure to this level for 18 d, mortality increased; however, there was no increase after 63-d exposure.

TABLE S-1

SUMMARY OF STUDIES OF ANIMAL EXPOSURE TO ACROLEIN UP TO 2.5 mg/m^3*

Level	Time	Species	Effects
2.3	up to 91 d	RAT	Decreased wt. gain and vanillylmandelic acid levels; no effect on hematological values or respiratory resistance; slight loss of bronchial ciliation on days 7-35; perivascular edema after 35 d.
2.3	90 d	DOG MKY GPG RAT	Decreasing ocular and nasal discharge in DOG and MKY; no effect on wt. gain (except RAT, which decreased) or hematological values; various degrees of pulmonary inflammation in DOG, GPG, and RAT; parasitic infection in MKY; occasional, slight liver damage in DOG and GPG; kidney inflammation in DOG.
2.3	81 h	RAT	No effect on: liver-to-body-wt. ratio; adrenal and lung wt.; and liver, lung, and serum AP activity.
2.3	2 h	GPG	Significantly increased respiratory resistance and rate and decreased tidal volume.
1.6	8 h/d, 5 d/wk, 6 wk	RAT GPG MKY DOG	No effect on behavior, body wt. gain, hematological values, various enzyme activities; mild chronic lung inflammation; occasional emphysema; no definite alteration of respiratory epithelia or the peribronchial smooth musculature.
1.52	24 d	RAT	Progressive deterioration of general condition; 7/10 died; changes in magnitude and latent period of conditioned motor response; decreased blood cholinesterase activity and increased leukocytes, returning to normal by 20 d post-exposure; lung inflammation; myocardium and liver changes.
1.23-1.47	6 mo	RAT	Decreased body wt.; alveolar damage; liver cell damage; no effect on alveolar macrophages, spleen, kidney, stomach, or heart.

* This level, about 10 times the threshold limit value, was chosen arbitrarily.

TABLE S-1 (continued)

Level	Time	Species	Effects
1.4	2 h	GPG	Increased expiratory flow resistance and tidal volume and decreased respiration rate, max. change in 30-60 min.
1.24-1.31	10-180 d	RAT	Decreased number of alveolar macrophages on days 10-26; no effect on relative no. of cells, viability, and physiological activity; no effect on days 60-180.
1.24-1.31	15,18, 21, 26 32, 60, 63, or 77 d	RAT	Increased lung-to-body-wt. ratio only on day 77; no effect on various enzyme activities; decreased body wt. during 21-d exposure; no effect on no. of pregnant rats or no. and avg. wt. of fetuses for 26-d exposure; significantly increased mortality when a high bacterial dose followed an 18-d exposure, but not after a 63-d exposure.
0.93	6 h/d, 5 d/wk, 13 wk	RBT HAM	No effect on behavior, growth, food intake, hematological values, blood chemistry, urinalysis, organ-to-body-wt. ratios, gross autopsy, or histopathology of the respiratory tract.
0.9	2 h	GPG	Significantly increased total respiratory resistance; decreased respiratory rate.
0.74	61 d	RAT	General state and wt. affected by 6th wk in healthy rats and by 5th wk in rats with experimentally induced silicosis; changes in chronaxy of antagonistic muscles in both groups.
0.51	90 d	DOG GPG MKY RAT	No effect on behavior, wt. gain, hematological values, gross autopsy (RAT, MKY, GPG, DOG, with exceptions noted below). MKY & GPG & DOG - nonspecific inflammatory changes in liver, lung, kidney, and heart. DOG - some of the following: emphysema, lung congestion, some bronchiolar construction, hyperplasia of the thyroid, focal subcapsular hemorrhage of the spleen.

TABLE S-1 (continued)

Level	Time	Species	Effects
0.51	61 d	RAT	No change in behavior or general condition; lost wt.; loss of conditioned reflexes after 10 d; disturbance of spatial relationships; decreased urine coproporphyrin levels and blood cholinesterase activity; recovery post-exposure; some histopathologicial changes in the bronchi.
0.47	2 h	GPG	Slight increase in total respiratory flow resistance; slight decrease in respiratory rate and minute volume.
0.15	61 d	RAT	No change in behavior, general condition, wt., magnitude or latent period of conditioned motor reflexes, urine coproporphyrin levels, or blood cholinesterase activity; no appreciable changes found on autopsy.
0.14	61 d	RAT	Changes in chronaxy of antagonistic muscles in healthy rats and rats with silicosis.
0.03	61 d	RAT	No change in a variety of biological, biochemical, and physiological tests in healthy rats or rats with silicosis.

Gusev et al. (1966) found no toxic effects after 61-d exposure to 0.15 mg/m^3, minor neurological effects after 0.51 mg/m^3, and severe effects, with 70% mortality, after 1.52 mg/m^3. Sinkuvene (1970) found no effects after 61 d at 0.03 mg/m^3, minor changes (of dubious toxicological significance) at 0.14 mg/m^3, and severe toxicity at 0.74 mg/m^3.

Feron et al. (1978) exposed rats 6 h/d, 5 d/wk, for 13 weeks. At 0.93 mg/m^3, growth retardation was not statistically significant, but was toxicologically important because of its consistency. Higher doses (3.3 mg/m^3 and 11.4 mg/m^3) were definitely toxic with decreased weight gain, pathologic changes in respiratory epithelia, and other effects. Intermediate doses of 1.23 to 1.47 mg/m^3 for 6 mo (Roussel et al., 1973) caused decreased body weight gain, alveolar damage, liver cell damage, and had no effect on alveolar macrophage activity or other major organs.

Guinea pig studies: Murphy et al. (1963) studied respiratory physiology (see Table III-8). They found minor, possibly unimportant, changes after 2 h of 0.47 mg/m^3 of acrolein and definite respiratory effects (increased resistance, decreased rate, etc.) at doses of 0.9 mg/m^3 and higher.

Lyon et al. (1970) exposed guinea pigs for 90 d (see Table III-9). The low concentration of 0.51 mg/m^3 was probably nontoxic (only nonspecific inflammatory changes in various organs were reported). Doses of 1.6 mg/m^3 and up caused pulmonary pathology and other effects.

Larger animal studies: Denine (1971) gave chickens large, brief (5 min/d) doses and found dose-related toxicity, but did not determine a no-effect dose (Table III-10).

Feron et al. (1978) exposed rabbits 6 h/d, 5 d/wk for 13 wk (Table III-12). They found no effects at 0.93 mg/m^3, occasional sneezing and decreased feed intake and weight gain at 3.3 mg/m^3, and histopathology of the respiratory epithelia at 11.4 mg/m^3.

Iwanoff (1911) gave cats very toxic doses (Table III-13) of 25-210 mg/m^3. The symptoms of irritation were immediate and increased in severity with time. All apparently recovered within a few days.

Lyon et al. (1970) exposed squirrel monkeys (Table III-14) and dogs (Table III-15) to acrolein either continuously for 90 d or 8 h/d, 5 d/wk, for 6 wk. With the monkeys, 0.51 mg/m^3 had no definite effects, while 1.6 mg/m^3 caused some pulmonary inflammation. Dogs were more sensitive since the low dose of 0.51 mg/m^3 did cause pulmonary pathology in two of four dogs.

HUMAN EXPOSURES

People can be exposed to acrolein in ambient air and in cigarette smoke. These exposures and human experimental exposures are discussed here, followed by examples of regulations and recommendations for limiting human exposure.

Ambient air levels: Measured background levels of acrolein in urban areas to which the general public can be exposed are listed in Table S-2. They are all concentrations determined outdoors. No examples of indoor air levels were found.

TABLE S-2

EXAMPLES OF AMBIENT AIR LEVELS OF ACROLEIN

Level (mg/m^3)	Location	Reference
0.005-0.025	At street level in South Pasadena, CA; July-November	Renzetti and Bryan (1961)
0.002-0.025	At sixth-floor level in Los Angeles, CA; September-November	Renzetti and Bryan (1961)
0.023	Urban polluted air	Stupfel (1976)
0.016	Downtown Los Angeles; September-October	Altshuller (1978)
0.014	Urban air	Criteria for Community Air Quality Committee (1968)
0.014	Huntington Park, CA; October	Altshuller (1978)

Cigarette smoke: Cigarette smoke is a frequent confounding factor in studies of human exposure to acrolein both because of the respiratory irritant effects of whole smoke and the presence of acrolein in the smoke. Estimates of acrolein levels vary with the type of cigarette and the researcher. Table S-3 cites some examples found in the literature. Using the highest reported level of 20 µg/puff (Kensler and Battista, 1963), one can estimate that a smoker's lungs will be momentarily (but repeatedly) exposed to air containing ~ 28.6 mg acrolein/m^3 (20 µg/0.7 L tidal lung volume). This concentration is one hundred times greater than the TLV of 0.25 mg/m^3.

TABLE S-3

ACROLEIN LEVELS IN CIGARETTE SMOKE

Level	Reference
7-12 μg/35 mL puff (200 to 343 mg/m^3)	Horton and Guerin (1974)
2.9-8.2 μg/40 mL puff (72.5-205 mg/m^3)	Newsome et al. (1965)
112 μg/cigarette	Haroz and Mattenberger-Kreber (1977)
3.6 μg/35 mL puff (103 mg/m^3)	Bridges et al. (1977)
60 ppm (138 mg/m^3)	Stupfel (1976)
7-74 μg/cigarette; 9-10 puff/cigarette	Rylander (1973)
20 μg/40 mL puff (500 mg/m^3)	Kensler and Battista (1963)

Experimental studies: A wide variety of experimental studies in humans is fully described in Table IV-1, and summarized here in Table S-4. Many are not very useful because they involve mixtures of noxious gases. Others show that humans will tolerate 5-10 mg/m^3 of acrolein for only a minute or two, but these are also of minimal use for our purpose.

Several important studies have, however, determined thresholds for specific effects. Plotnikova (1960) found that 0.6 mg/m^3 was the threshold for an acrolein-induced increase in photosensitivity of the eye. Weber-Tschopp et al. (1977) found a threshold of about 0.2 mg/m^3 for both subjective ("annoyance") and objective (blinking frequency) responses in people subjected to increasing concentrations of acrolein. Odor thresholds include 0.49 mg/m^3 ("recognition"; Leonardos et al., 1969), 0.078 mg/m^3 (Ubaidullaev and Abramova, 1976), and 0.07 mg/m^3 (Sinkuvene, 1970).

Exposures of the general public: No useful occupational (Table V-1) or accidental (Table V-2) studies were found.

International standards and recommendations: Many countries have regulations concerning the levels of acrolein allowed in the workplace or the

TABLE S-4

SUMMARY OF ACUTE HUMAN EXPERIMENTAL EXPOSURE TO ACROLEIN

Acrolein Level (mg/m^3)	Effects
2.3-5.4	Medium to severe eye irritation in 5 min.
4	Irritation of the conjuctiva, nasal mucosa, and nasopharyngeal region.
3.0-3.7	Medium to severe eye irritation in 5 min.
2.8	Extremely irritating to all mucous membranes in 5 min; lacrimation.
2.3	82% of the exposures caused medium or severe eye irritation in 5 min.
1.75-2.0	Changes in amplitude of respiratory movements; slightly increased respiratory frequency; decreased eye sensitivity to light; changes in optical chronaxy.
1.88	Only just tolerable for 10 min; extremely irritating to all mucous membranes.
1.5	Slight changes in amplitude of respiratory movements.
0-1.5	No effect on rheobase or optical chronaxy; irritation and annoyance increasing with concentration to severe eye and moderate nose irritation; indications of possible adaptation at lower levels and sensitization at higher levels.
1.2	Medium or severe eye irritation, numbers of complaints varying with length and type of exposure; tear volume, pH, and lysozyme activity changed.
0.8-1.05	Slight eye and nose irritation; no effect on respiratory frequency or amplitude; odor perceived.
0.8-0.83	Increased eye sensitivity to light in 5 min; eye irritation in 70% of the subjects in 2 min; minimum odor perceived by 9/10 was 0.8 mg/m^3.
0.7	Some eye, nose, and throat irritation for 40 min, then decreased; 20% decrease in respiratory frequency in 40 min; subjective air quality decreased for 20 min, then increased.
0.6-0.65	Threshold value for action on eye sensitivity to light.
0.49-0.5	Subthreshold value for eye sensitivity to light; lowest level at which all recognized the odor.
0.33-0.35	30% felt eye irritation in 2 min; increased annoyance and almost no eye or nose irritation during repeated exposures.
0.23	50% detected the odor.
0.14	Odor threshold; slight eye irritation.
0.07-0.078	Odor threshold for most acrolein-sensitive people.
0.05	Threshold for affecting electrocortical activity.
0.03	Subthreshold for affecting electrocortical activity.

ambient air. Studies have also recommended safe levels for different situations. Table S-5 summarizes this information. Allowable levels in work environments range from 1.0 mg/m^3 for a ceiling level to 0.25 mg/m^3 as the most common avg. TLV. Only one indoor recommendation was found--0.1 mg/m^3 in the USSR. Ambient air standards range from 0.03 mg/m^3 to a recommended 0.005 mg/m^3.

RECOMMENDED RANGE OF CONCERN

From the animal data, a concentration of 1 mg/m^3 is quite definitely toxic. The most common "no-effect" level was about 0.5 mg/m^3. From these data, this would be the upper level of concern. However, acrolein appears to have additive effects with other irritants (such as HCHO), the evidence on sensitization/tolerance is contradictory, and few interspecies studies were done. These problems suggest recommending a lower value for the upper range of concern.

From the human exposure data the main noxious characteristic of acrolein is its sharp, irritating odor. The irritation threshold appears to be 0.1-0.2 mg/m^3, and the odor threshold somewhat below 0.1 mg/m^3. No effects at all were seen below 0.05 mg/m^3. To allow for the fact that the effects of acrolein appear to be additive with other irritants and to allow a margin of error, we suggest a range of concern of 0.1 to 0.01 mg/m^3. However, there should be some sort of an additivity system for the various irritants (HCHO, SO_2, NH_3, etc.); the TLV system is suggested.

TABLE S-5

SUMMARY OF REGULATIONS AND RECOMMENDATIONS FOR LIMITING HUMAN EXPOSURE TO ACROLEIN

Level (mg/m^3)	Recommendation/Regulation	Reference
1.0	Standard for occupational exposure in Czechoslovakia (ceiling).	SRC (1979); ILO (1970)
0.8	Tentative short-term-exposure-limit for the workplace.	ACGIH (1980)
0.7	Standard for occupational exposure in Hungary and USSR.	SRC (1979)
0.5	Standard for occupational exposure for Czechoslovakia (avg.) and Romania (ceiling).	SRC (1979); ILO (1970)
0.3	Standard for occupational exposure in Romania (avg.).	SRC (1979)
0.25	Standard for occupational exposure in Australia, Belgium, Finland, West Germany, Japan, The Netherlands, Sweden, Switzerland, and Yugoslavia, and East Germany.	SRC (1979); Jermini and Weber (1975); Bittersohl (1974)
0.25	8-h TLV set by OSHA; time-weighted avg. TLV recommended by ACGIH.	SRC (1979); ACGIH (1980)
0.1	Max. acceptable room air concentration in the U.S.S.R.	Kettner (1978)
0.046	Recommended lowest concentration necessary for TLV.	Kane et al. (1979)
0.03	Max. immission concentration for populated places in U.S.S.R.--both avg. and one-time.	U.S.S.R. (1972); Kettner (1978)
0.023	Recommended concentration below which no sensory irritation will occur.	Criteria for Community Air Quality Committee (1968)
0.005	Recommended highest concentration for an Air Quality Standard.	Kane et al. (1979)

SECTION I

INTRODUCTION

This report was compiled as the sixth of several tasks under Contract No. 68-03-2928, "Health Effects Support for the Emission Control Technology Division (U.S. Environmental Protection Agency, Ann Arbor, Michigan)." The goal of the project is to evaluate health effects literature on specific compounds emitted from automobiles equipped with emission-control devices (specifically catalytic converters), not for the purpose of creating a criteria document but to identify a range of concern or a no-observable-effect level for each compound to serve as guidance to automobile manufacturers in their development of future emission-control devices.

The present report was meant to be largely a series of charts or tables of pertinent data with the tests logically ordered according to exposure levels. The narrative summary was not meant to describe again each paper in detail. There are admittedly some disadvantages in not doing so; e.g., some of the gradations in effect that the authors of a particular paper observed may be diluted or lost when the details are spread throughout an exceptionally large table, or between several tables. Papers described in a largely narrative fashion, however, often are difficult to compare. Results that appear within their source paper to be quite definitive may appear less so or even anomalous when juxtaposed in tabular format with other results from similar studies. Hence, the present format was designed to facilitate comparisons.

Literature related to health effects of inhaled acrolein was collected mainly by computer search of TOXLINE and TOXBACK and manual search through major review articles on acrolein. Approximately 125 papers and other documents were evaluated, but only about 45 contained original data suitable for tabulation.

Experimental animal and human exposure studies and bioassay studies were evaluated and summarized by senior Ph.D. pharmacologists. Occupational exposures were rated by an epidemiologist with an M.D. degree. Figure I-1 is the form used for rating documents by the project pharmacologist and epidemiologist. Each document was rated in a two-step procedure according to the applicability of its subject matter and to the quality of the experimental methodology. The letter assigned in rating the document A, B, C, or D was derived from the corresponding lower case letters under item 7 in Figure I-1. Thus, a study was rated A if it directly applies to or assists in establishing a range of concern for exposure to acrolein.

CHECK WHERE APPROPRIATE:	PAPER DEFECTIVE 0	PAPER IS SUB-STANDARD 1	STANDARD QUALITY 2	SUPERIOR PAPER 3
1. Do they state/limit the problem?				
2. Adequacy of sample				
3. Replicability				
4. Controls/control procedures				
5. Completeness and comprehensibility of results				
6. Validity of conclusions, interpretation of data				

7. Applicability to health effects of acrolein as guidance for establishing a range of concern for acrolein in automobile exhaust. (circle one)

a. Clearly, directly applies/assists in establishing a range of concern. (Chronic human studies; acute exposure of humans if minimal effects.)

b. Research requires major inferences; potentially applicable. (Chronic animal studies; acute human, maximal effect; acute animal, minimal effects.)

c. Useful hints or suggestions; tentatively applicable. (Acute animal, lethal effects; studies in above categories but effects reported not appropriate.)

d. Not directly applicable (peripheral useful information).

Figure I-1. Form for report rating.

The second part of the rating is the methodology score. The document reviewer checked off which score should be given for each of the first six items in Figure I-1, and the total was written at the top of the page along with the letter that rated the paper's applicability. In some cases, such as reviews, theoretical papers, and low-rated foreign language documents, a paper may have received an applicability rating (generally C or D) but none on methodology.

Data, including the MRI-assigned rating, from the A-, B-, and some C-rated papers were tabulated by mid-level scientists. Information for each topic heading was carefully sought; so if blanks appear in the table, the reader can generally assume the data were not given. Information which was unclear in the original document but needed for tabulation is preceded in the tables by a qualifying word such as "apparently." Sometimes a group published several papers that described the same tests. To avoid redundancy, all pertinent papers were cited and the test was described as well as possible from all the papers' descriptions.

The final written summary of the tabulated data was also performed by a senior pharmacologist. This summary attempts to reflect objectively the scientific community's thought as a whole and does not reflect the tabular material by weight. The tables reflect the amount of data generated, and the summary puts the evaluated data in perspective with the overall scientific community's opinions.

The references are cited in an annotated bibliography that includes not only each document's rating but also a brief comment on its pertinence (or lack of same) to the study. English titles are given for foreign language documents, and an abbreviation of the language is given in parentheses at the end of the citation.

The report is organized into the following chapters: II. Bioassay Tests, III. Experimental Animal Inhalation Exposures, IV. Experimental Human Inhalation Exposures, and V. Other Human Exposures. The Summary precedes the entire report and the Annotated Bibliography follows it.

SECTION II

BIOASSAYS

Only five *in vitro* studies using respiratory tissues and gaseous acrolein were found in the literature. The results, described in Table II-1, appear to have little information directly useful to this task on determining a range of concern for human exposure to acrolein in automobile exhaust. The data are discussed in the Summary.

TABLE II-1. RESPIRATORY TRACT BIOASSAYS

Compound and concentration in mg/m^3 (ppm)	Temperature and humidity	Preparation exposed	Description of tests and duration	Results	Reference and rating
Acrolein 1,250	37°C	Tracheal tissue from young adult New Zealand albino rabbits.	The concentration of acrolein (in air) per puff producing 50% inhibition in tracer particle movement, after 8-40 mL, 12 sec "puffs" of air.	The "8 puff ED_{50}" was 50 µg/puff, or 1,250 mg/m^3. The authors' value for acrolein levels in cigarette smoke was 20 µg/puff.	Kensler and Battista (1963) D-10
Acrolein 875-1,000		White Leghorn chickens.	The larynx of an anesthetized chicken was lifted into its mouth. The animal was exposed to a 40-mL puff for 4 sec, once every minute. After each exposure, the ciliary transport rate of tracer particles was measured. The level of acrolein/puff which would cause a 50% inhibition after 8 puffs was determined.	The "8 puff ED_{50}" was 35-40 µg/puff, or 875-1,000 mg/m^3. Cigarette smoke is estimated to contain 8.2 - 20 µg acrolein/40 mL puff.	Battista and Kensler (1970) C-9
Acrolein 31.2-247.8		Rabbit tracheal sections.	HCHO from an air nebulizer was added to a moist, temperate chamber at the rate of 54 L/h for a maximum of 60 min. Ciliary beating was monitored (method not given) during exposure, but no recovery period was included.	Ciliary activity stopped after ~ 6 min exposure to 247.8 mg/m^3. Decreasing concentrations caused increasing time to ciliostasis, ~ 36 min for 31.2 mg/m^3.	Dalhamn and Rosengren (1971) C-5
Acrolein 140		Not explicit as to which system was used with acrolein: *in vivo* measures on exposed canine tracheal cilia, or *in vitro* measures on cilia from sheep, goat, and rat tracheal preparations.	Ciliary activity was observed during a ~ 12-min exposure to gaseous acrolein.	Ciliary movement stopped in 11 min 10 sec. When mixed with 2,150 mg acetaldehyde/m^3, movement stopped in 5.5 min about the same length of exposure required for whole cigarette smoke.	Guillerm et al. (1961) C-7
Acrolein 81.6 (35)	37° C, "saturated with water"	Alveolar macrophages from Hartley guinea pigs.	Macrophages were deposited on membrane filters, which were then placed on a nutrient liquid. Exposed to acrolein in air for 30 min, then the ATP level in the cells was measured. Authors believe this method reproduces the bronchial and alveolar microenvironment.	Caused a 30-70% decrease in the level of ATP, compared to controls.	Voisin et al. (1979) C-9 Voisin et al. (1980) C-9

(continued)

TABLE II-1 (concluded)

Compound and concentration in mg/m^3 (ppm)	Temperature and humidity	Preparation exposed	Description of tests and duration	Results	Reference and rating
Acrolein 28	See entry in this table for exposure to 81.6 mg/m^3 (Voisin et al., 1979) for details of the methodology.			Caused a 25-50% decrease in ATP levels, compared to controls.	Voisin et al. (1979) C-9 Voisin et al. (1980) C-9
Acrolein 18.6 (8)	See entry in this table for exposure to 81.6 mg/m^3 (Voisin et al., 1979) for details of the methodology.			Caused a 20-45% decrease in ATP levels, compared to controls.	Voisin et al. (1979) C-9 Voisin et al. (1980) C-9
Acrolein 9.3 (4)	See entry for exposure to 81.6 mg/m^3 (Voisin et al., 1979) for the details of the methodology.			Caused a 0-21% decrease in ATP levels, compared to controls.	Voisin et al. (1979) C-9 Voisin et al. (1980) C-9

SECTION III

EXPERIMENTAL ANIMAL INHALATION EXPOSURES

The essential parameters of numerous animal inhalation exposure experiments are tabulated in this section. The primary organization of data is by species, in order of increasing weight (mice to dogs in this case). Within a species, studies are divided by dosing duration: acute exposure ($\leq$ 24 h), repeated exposure, and chronic exposure (> 90 d). Within a single table, reported results are listed in order of decreasing exposure level. The studies are discussed in the Summary.

The tables have been arranged in the aforesaid manner for the following reasons: (a) there were about 120 separate tests tabulated; (b) there are distinct differences in lung anatomy among the laboratory species used, and the differences seen in their relative responses may have been largely due to these anatomical differences; and (c) by putting the highest concentrations and worst effects first, one can more readily understand the significance of minor or less-severe changes occurring at lower levels. However, a condensation of the data by acrolein concentration is in Table III-16.

In the animal exposure tables in this section, the column headed Total Length of Experiment includes not only the total length of exposure to acrolein but also any recovery time observed in the study. This recovery time was included to note the endurance or reversibility of the toxic effects.

TABLE III-1. MICE--ACUTE EXPERIMENTAL EXPOSURE TO ACROLEIN

Compound(s) and Concentration(s), mg/m³ (ppm)	Mode of Exposure	Species/Strain/ Age/Weight	No. of Test Animals	No. of Controls	Duration and Frequency of Exposure	Total Length of Experiment	Effects	Reference and Rating
Acrolein 600		Swiss mice, 15-25 g, anesthetized, with tracheal cannula	5 M	5 M	5 min	5 min	Decreased pulmonary resistance, respiratory minute volume, and respiratory frequency. No change in respiratory compliance.	Watanabe and Aviado (1974) C-9
Acrolein 300		Swiss mice, 15-25 g, anesthetized, with tracheal cannula	5 M	Apparently served as own controls	5 min	5 min	Decreased pulmonary compliance, pulmonary resistance, tidal volume, and respiratory frequency (statistical significance not given).	Watanabe and Aviado (1974) C-9
Acrolein 277 (119)	Inhalation chamber	Mice	44	20	6 h	6 h	100% mortality.	Philippin et al. (1969) C-8
Acrolein 186 (80)	Inhalation chamber	Mice	24	20	6 h	6 h	75% mortality	Philippin et al. (1969) C-8
Acrolein 142 (61)	Inhalation chamber	Mice	20	20	6 h	6 h	40% mortality.	Philippin et al. (1969) C-8
Acrolein 93.2 (40)	Inhalation chamber	dd strain mice, 20 ± 3 g	? M	? M	15 min or 1 h (text is unclear)	7 d	Marked respiratory difficulty, decreased respiration rate. ~ 20% decrease in body wt. 2 d after exposure. Then gradual wt. increase to pre-exposure level by 5 d post-exposure.	Iwasaki (1979) D--

(continued)

TABLE III-1. (continued)

Compound(s) and Concentration(s), mg/m^3 (ppm)	Mode of Exposure	Species/Strain/ Age/Weight	No. of Test Animals	No. of Controls	Duration and Frequency of Exposure	Total Length of Experiment	Effects	Reference and Rating
Acrolein 72.2 (31)	Inhalation chamber	Mice	20	20	6 h	6 h	No deaths.	Philippin et al. (1969) C-8
Acrolein 26.1 (11.2)	Inhalation chamber	Swiss-Webster mice, specific pathogen free, 20-30 g	4 M	Served as own controls	10 min	10 min	A maximum decrease in respiratory rate of 80.5%. A different group of mice with repeated previous exposures to 0.40 mg/m^3 before exposure to 26.1 mg/m^3 had a 73.7% decrease. The results of this entire series of expts. (see entries below and in Table II-2.) suggest that a slight but definite tolerance to acrolein develops after repeated, low (0.40 mg/m^3) exposures.	Kane and Alarie (1977) B-12
Acrolein ~ 20.63 (8.97) HCHO ~ 12.16 (9.73)	Inhalation chamber	Swiss-Webster mice, specific pathogen free, 20-30 g	4 M	Served as own controls	10 min, once	10 min	Maximum decrease of respiratory rate was 74.4%.	Kane and Alarie (1978) B-10
Acrolein ~ 18.31 (7.96) HCHO ~ 5.61 (4.49)	Inhalation chamber	Swiss-Webster mice, specific pathogen free, 20-30 g	4 M	Served as own controls	10 min, once	10 min	Maximum decrease in respiratory rate was 71.3%.	Kane and Alarie (1978) B-10

(continued)

TABLE III-1. (continued)

Compound(s) and Concentration(s), mg/m^3 (ppm)	Mode of Exposure	Species/Strain/ Age/Weight	No. of Test Animals	No. of Controls	Duration and Frequency of Exposure	Total Length of Experiment	Effects	Reference and Rating
Acrolein ~ 18.15 (7.89) HCHO ~ 0.99 (0.79)	Inhalation chamber	Swiss-Webster, mice, specific pathogen free, 20-30 g	4 M	Served as own controls	10 min, once	10 min	Maximum decrease in respiratory rate was 77.9%.	Kane and Alarie (1978) B-10
Acrolein 13.0 (5.6)	Inhalation chamber	Swiss-Webster mice, specific pathogen free, 20-30 g	4 M	Served as own controls	10 min	10 min	A maximum decrease in respiratory rate of 76.0%. A different group of mice with repeated previous exposures to 0.40 mg/m^3 before exposure to 13 mg/m^3 had 61.5% decrease.	Kane and Alarie (1977) B-12
Acrolein 12.47 (5.35)	Inhalation chamber	Swiss-Webster mice, specific pathogen free, 20-30 g	4 M	Served as own controls	10 min	10 min	A maximum decrease in respiratory rate of 70.1%. A different group of mice with repeated previous exposures to 0.40 mg/m^3 before exposure to 12.47 mg/m^3 had a 67.3% decrease.	Kane and Alarie (1977) B-12
Acrolein 7.2 (3.1)	Inhalation chamber	Swiss-Webster mice, specific pathogen free, 20-30 g	4 M	Served as own controls	10 min	10 min	A maximum decrease in respiratory rate of 65.7%. A different group of mice with repeated previous exposures to 0.40 mg/m^3 before exposure to 7.2 mg/m^3 had a 53.0% decrease.	Kane and Alarie (1977) B-12
Acrolein ~ 4.72 (2.05) HCHO ~ 3.13 (2.50)	Inhalation chamber	Swiss-Webster mice, specific pathogen free, 20-30 g	4 M	Served as own controls	10 min, once	10 min	Maximum decrease in respiratory rate was 61.8%.	Kane and Alarie (1978) B-10

(continued)

TABLE III-1. (continued)

Compound(s) and Concentration(s), mg/m³ (ppm)	Mode of Exposure	Species/Strain/ Age/Weight	No. of Test Animals	No. of Controls	Duration and Frequency of Exposure	Total Length of Experiment	Effects	Reference and Rating
Acrolein 2.3-4.7 (1-2) were challenged for 30 min, prior to acrolein exposure, by aerosol inhalation of radiolabeled bacterial suspensions of Proteus mirabilis and Staphylococcus aureus.	Inhalation chamber	Swiss albino mice (CD-1 strain), 18-20 g	18-24 M	18-24 M; also exposed to the bacteria	4 or 24 h	24 h	Mild discomfort, indicated by eye blinking and rubbing of the nose. Decreased pulmonary bactericidal activity from normal (percent of initial viable S. aureus and P. mirabilis remaining in the lungs of the test mice was greater). The difference was not significant at 4 h, but was at 24 h. Bactericidal activity was more inhibited for P. mirabilis (~ 50% remaining versus ~ 0.3% for controls) than for S. aureus (~ 9-20% versus ~ 0.4% for controls). Compare with the following results for additional exposure to viruses.	Jakab (1977) C-12
Acrolein 2.3-4.7 (1-2) Given an aerosol of para-influenza 1 (Sendai) virus at 2.5 x 10^8 infective dose/mL, 7 d before acrolein exposure. Then a 30-min exposure to an aerosol of radiolabeled bacterial suspensions of Proteus mirabilis and Staphylococcus aureus, immediately before acrolein exposure. Both test and control animals.	Inhalation chamber	Swiss albino mice (CD-1 strain), 18-20 g	18-24 M	18-24 M	4 or 24 h	24 h	Discomfort to the nose and eyes. Labored breathing. By 24 h, some mice appeared to be moribund. The pulmonary bactericidal activity at 24 h was decreased for the acrolein-exposed group for S. aureus (proliferation to 250 ± 60% versus 42 ± 7% remaining in the controls). The adverse effect was even more pronounced for P. mirabilis (proliferation to 6,800 ± 4,000% versus 1,400 ± 350% for the controls). Compare with the results for exposure without viral infection or with a lower viral exposure (Jakab, 1977).	Jakab (1977) C-12

(continued)

TABLE III-1. (continued)

Compound(s) and Concentration(s), mg/m^3 (ppm)	Mode of Exposure	Species/Strain/ Age/Weight	No. of Test Animals	No. of Controls	Duration and Frequency of Exposure	Total Length of Experiment	Effects	Reference and Rating
Acrolein 2.3-4.7 (1-2) Given an aerosol of para-influenza 1 (Sendai) virus at 10^7 infective dose/mL, 7 d before acrolein exposure. Then for the 30 min prior to acrolein exposure were exposed to an aerosol of radiolabeled bacterial suspensions of Proteus mirabilis and Staphylococcus aureus.	Inhalation chamber	Swiss albino mice (CD-1 strain), 18-20 g	18-24 M	18-24 M; also exposed to virus and bacteria	4 or 24 h	24 h	Discomfort to nose and eyes. Labored breathing. The pulmonary bactericidal activity at 24 h was decreased in the acrolein-exposed group for S. aureus (82 ± 22% remaining versus 8 ± 2% for the controls). The adverse effect was even more pronounced for P. mirabilis (proliferation to 1,500 ± 600% versus 82 ± 49% remaining for the controls). Compare with the results for exposures with no viral infection or with a higher viral exposure (Jakab, 1977).	Jakab (1977) C-12
Acrolein ~ 4.30 (1.87) HCHO ~ 1.78 (1.42)	Inhalation chamber	Swiss-Webster mice, specific pathogen free, 20-30 g	4 M	Served as own controls	10 min, once	10 min	Maximum decrease in respiratory rate was 60.7%.	Kane and Alarie (1978) B-10
Acrolein 4.26 (1.83)	Inhalation chamber	Swiss-Webster mice, specific pathogen free, 20-30 g	4 M	Served as own controls	10 min	10 min	A maximum decrease in respiratory rate of 51.9%. A different group of mice with repeated previous exposures to 0.40 mg/m^3 before exposure to 4.26 mg/m^3 had a 30.1% decrease.	Kane and Alarie (1977) B-12

(continued)

TABLE III-1. (continued)

Compound(s) and Concentration(s), mg/m^3 (ppm)	Mode of Exposure	Species/Strain/ Age/Weight	No. of Test Animals	No. of Controls	Duration and Frequency of Exposure	Total Length of Experiment	Effects	Reference and Rating
Acrolein 4.0 (1.7)	Inhalation chamber	Swiss-Webster mice, specific pathogen free, 20-30 g	Groups of 4 M	Served as own controls	10 min	~ 20 min, with 5-min pre- and post-exposure periods	This concentration causing a 50% decrease in respiration rate (RD_{50}), was calculated from the results of exposures of groups of mice to ~ 0.1-~ 10 ppm. Exposure of mice through tracheal cannulae caused much smaller decreases in respiration rate (e.g., one level causing a 61% decrease in uncannulated mice and a 3.7% decrease in cannulated mice), indicating that the site of reactions provoking the decreases is in the upper respiratory tract.	Kane and Alarie (1977) B-12
Acrolein ~ 4.00 (1.74) HCHO ~ 4.30 (3.44)	Inhalation chamber	Swiss-Webster mice, specific pathogen free, 20-30 g	4 M	Served as own controls	10 min, once	10 min	Maximum decrease in respiratory rate was 62.0%.	Kane and Alarie (1978) B-10
Acrolein 2.70 (1.16)	Inhalation chamber	Swiss-Webster mice, specific pathogen free, 20-30 g	4 M	Served as own controls	10 min	10 min	A maximum decrease in respiratory rate of 46.6%. A different group of mice with repeated previous exposures to 0.40 mg/m^3 before exposure to 2.7 mg/m^3 had a 19.9% decrease.	Kane and Alarie (1977) B-12
Acrolein ~ 1.68 (0.73) HCHO ~ 8.96 (7.17)	Inhalation chamber	Swiss-Webster mice, specific pathogen free, 20-30 g	4 M		10 min, once	10 min	Maximum decrease in respiratory rate was 69.6%.	Kane and Alarie (1978) B-10

(continued)

TABLE III-1. (continued)

Compound(s) and Concentration(s), mg/m^3 (ppm)	Mode of Exposure	Species/Strain/ Age/Weight	No. of Test Animals	No. of Controls	Duration and Frequency of Exposure	Total Length of Experiment	Effects	Reference and Rating
Acrolein ~ 1.56 (0.68) HCHO ~ 3.13 (2.50)	Inhalation chamber	Swiss-Webster mice, specific pathogen free, 20-30 g	4M	Served as own controls	10 min, once	10 min	Maximum decrease in respiratory rate was 52.8%.	Kane and Alarie (1978) B-10
Acrolein ~ 1.29 (0.56) HCHO ~ 1.08 (0.86)	Inhalation chamber	Swiss-Webster mice, specific pathogen free, 20-30 g	4 M	Served as own controls	10 min, once	10 min	Maximum decrease in respiratory rate was 41.4%.	Kane and Alarie (1978) B-10
Acrolein 1.2 (0.52)	Inhalation chamber	Swiss-Webster mice, specific pathogen free, 20-30 g	4 M	Served as own controls	10 min	10 min	A maximum decrease in respiratory rate of 28.7%. A different group of mice with repeated previous exposures to 0.40 mg/m^3 before exposure to 1.2 mg/m^3 had a 24.1% decrease.	Kane and Alarie (1977) B-12
Acrolein 1.03 (0.44)	Inhalation chamber	Swiss-Webster mice, specific pathogen free, 20-30 g	4 M	Served as own controls	10 min	10 min	A maximum decrease in respiratory rate of 30.1%. A different group of mice with repeated previous exposures to 0.40 mg/m^3 before exposure to 1.03 mg/m^3 had a 14.8% decrease.	Kane and Alarie (1977) B-12

(continued)

TABLE III-1. (concluded)

Compound(s) and Concentration(s), mg/m^3 (ppm)	Mode of Exposure	Species/Strain/ Age/Weight	No. of Test Animals	No. of Controls	Duration and Frequency of Exposure	Total Length of Experiment	Effects	Reference and Rating
Acrolein ~ 0.85 (0.37) HCHO ~ 0.41 (0.33)	Inhalation chamber	Swiss-Webster mice, specific pathogen free, 20-30 g	4 M	Served as own controls	10 min, once	10 min	Maximum decrease in respiratory rate was 30.1%.	Kane and Alarie (1978) B-10
Acrolein 0.68 ± 0.25	Inhalation chamber	Swiss-Webster mice, specific pathogen free, 20-30 g	32 M; 8 groups of 4	Served as own controls	10 min	~ 20 min, with 5-min pre- and post-exposure periods	Caused a 31.1 ± 3.3% decrease in respiratory rate.	Kane and Alarie (1977) B-12
Acrolein ~ 0.28 (0.12) HCHO ~ 0.46 (0.37)	Inhalation chamber	Swiss-Webster mice, specific pathogen free, 20-30 g	4 M	Served as own controls	10 min, once	10 min	Maximum decrease in respiratory rate was 20.2%.	Kane and Alarie (1978) B-10

TABLE III-2. MICE--REPEATED DOSE EXPERIMENTAL EXPOSURE TO ACROLEIN

Compound(s) and Concentration(s), mg/m^3 (ppm)	Mode of Exposure	Species/Strain/ Age/Weight	No. of Test Animals	No. of Controls	Duration and Frequency of Exposure	Total Length of Experiment	Effects	Reference and Rating
Acrolein 14-116.5 (6-50)	Inhalation chamber	Mice	47	43	6 h/d, 5 d/wk, 2 wk; this schedule 1st at 14 mg/m^3, then 35 mg/m^3, then 58 mg/m^3; then one 6-h exposure to 116.5	6 wk	46.6% mortality after the final exposure (6 h at 116.5 mg/m^3). In the physical performance test (swimming), apparently a significant change only after exposure to 58 mg/m^3 (document is unclear). Exposed mice maintained a constant weight, below that of the controls, which regularly gained weight. 15 exposed (and 10 control) mice were sacrificed 24 h after the last exposure and the lungs examined: atelectasis, cellular inflammation, edematous inflammation, and thickening of the septa.	Philippin et al. (1969) C-8
Acrolein 100	Inhalation chamber	Swiss mice, avg. 21.2 g	5 M	8 M	30 min, twice daily; 5 wk	5 wk	Significantly decreased pulmonary compliance. Significantly increased serum antitrypsin activity and lung total phospholipids.	Watanabe and Aviado (1974) C-9
Acrolein 26.1 (11.2)	Inhalation chamber	Swiss-Webster mice, specific pathogen free, 20-30 g	8 M; exposed to 0.4 mg/m^3 for 3 h/d for the three previous days	Served as own controls?	10 min	4 d	A maximum decrease in respiration rate of 73.7%. A group of fresh mice exposed to this level for 10 min had a 80.5% decrease. The results of this entire series of expts. (see entries below and in Table II-1) suggests that a slight but definite tolerance to acrolein develops after repeated, low (0.40 mg/m^3) exposures.	Kane and Alarie (1977) B-12
Acrolein 13.0 (5.6)	Inhalation chamber	Swiss-Webster mice, specific pathogen free, 20-30 g	8 M; exposed to 0.4 mg/m^3 for 3 h/d for the three previous days	Served as own controls?	10 min	4 d	A maximum decrease in respiration rate of 61.5%. A group of fresh mice exposed to this level for 10 min had a 76% decrease.	Kane and Alarie (1977) B-12

(continued)

TABLE III-2. (continued)

Compound(s) and Concentration(s), mg/m^3 (ppm)	Mode of Exposure	Species/Strain/ Age/Weight	No. of Test Animals	No. of Controls	Duration and Frequency of Exposure	Total Length of Experiment	Effects	Reference and Rating
Acrolein 12.47 (5.35)	Inhalation chamber	Swiss-Webster mice, specific pathogen free, 20-30 g	8 M; exposed to 0.4 mg/m^3 for 3 h/d for the three previous days	Served as own controls?	10 min	4d	A maximum decrease in respiration rate of 67.3%. A group of fresh mice exposed to this level for 10 min had a 70.1% decrease.	Kane and Alarie (1977) B-12
Acrolein 7.2 (3.1)	Inhalation chamber	Swiss-Webster mice, specific pathogen free, 20-30 g	8 M; exposed to 0.4 mg/m^3 for 3 h/d for the three previous days	Served as own controls?	10 min	4 d	A maximum decrease in respiration rate of 53.0%. A group of fresh mice exposed to this level for 10 min had a 65.7% decrease.	Kane and Alarie (1977) B-12
Acrolein 4.26 (1.83)	Inhalation chamber	Swiss-Webster mice, specific pathogen free, 20-30 g	8 M; exposed to 0.4 mg/m^3 for 3 h/d for the three previous days	Served as own controls?	10 min	4 d	A maximum decrease in respiration rate of 30.1%. A group of fresh mice exposed to this level for 10 min had a 51.9% decrease.	Kane and Alarie (1977) B-12

(continued)

TABLE III-2. (continued)

Compound(s) and Concentration(s), mg/m^3 (ppm)	Mode of Exposure	Species/Strain/ Age/Weight	No. of Test Animals	No. of Controls	Duration and Frequency of Exposure	Total Length of Experiment	Effects	Reference and Rating
Acrolein 4.0 (1.7)	Inhalation chamber	Swiss-Webster mice, specific pathogen free, 20-30 g	4 M	Probably served as own controls (1st day pre-exposure values) for decrease in respiration values; a comparison group of 4 fresh mice exposed each day for 10 min	3 h/d, 4 d	4 d	One day 1, the maximum decrease in respiration rate (~ 40%) was reached in 5-6 min, and remained at that level for the entire exposure (the shape of a typical response curve for 10-min exposures to acrolein is this plateau). On day 2 the maximum response was ~ 50% decrease, maintained throughout the exposure. On days 3 and 4 the % decrease in respiration rate increased continuously throughout the exposure, to a maximum of ~ 70% at the end. This increase in the maximum response and change in the shape of the curve on days 3 and 4 indicates possible sensitization.	Kane and Alarie (1977) B-12
Acrolein 2.70 (1.16)	Inhalation chamber	Swiss-Webster mice, specific pathogen free, 20-30 g	8 M; exposed to 0.4 mg/m^3 for 3 h/d for the three previous days	Served as own controls?	10 min	4 d	A maximum decrease in respiration rate of 19.9%. A group of fresh mice exposed to this level for 10 min had a 46.6% decrease.	Kane and Alarie (1977) B-12
Acrolein 1.2 (0.52)	Inhalation chamber	Swiss-Webster mice, specific pathogen free, 20-30 g	8 M; exposed to 0.4 mg/m^3 for 3 h/d for the three previous days	Served as own controls?	10 min	4 d	A maximum decrease in respiration rate of 24.1%. A group of fresh mice exposed to this level for 10 min had a 28.7% decrease.	Kane and Alarie (1977) B-12

(continued)

TABLE III-2. (concluded)

Compound(s) and Concentration(s), mg/m^3 (ppm)	Mode of Exposure	Species/Strain/ Age/Weight	No. of Test Animals	No. of Controls	Duration and Frequency of Exposure	Total Length of Experiment	Effects	Reference and Rating
Acrolein 1.2 (0.5)	Inhalation chamber	Swiss-Webster mice, specific pathogen free, 20-30 g	4 M	Probably served as own controls (1st day pre-exposure values) for decrease in respiration values; a comparison group of 4 fresh mice was exposed each day for 10 min	3 h/d, 4 d	4 d	On day 1 and 2, the magnitude of the response (decrease in respiration rate) remained constant at ~ 30% during the 3-h exposure. (The shape of a typical response curve to a single one-time exposure is this plateau.) On day 3, the reponse continuously increased to ~ 55% at 8 min, leveled off for ~ 1 h, then continuously decreased to ~ 40% by the end of the exposure. On day 4, the response rose to a maximum of ~ 60% by ~ 10 min, and remained constant throughout the exposure. This increase in the maximum response and change in the shape of the curve on days 3 and 4 indicate possible sensitization.	Kane and Alarie (1977) B-12
Acrolein 1.03 (0.44)	Inhalation chamber	Swiss-Webster mice, specific pathogen free, 20-30 g	8 M; exposed to 0.4 mg/m^3 for 3 h/d for the three previous days	Served as own controls?	10 min	4 d	A maximum decrease in respiration rate of 14.8%. A group of fresh mice exposed to this level for 10 min had a 30.1% decrease.	Kane and Alarie (1977) B-12

TABLE III-3. HAMSTERS--ACUTE EXPERIMENTAL EXPOSURE TO ACROLEIN

Compound(s) and Concentration(s), mg/m^3 (ppm)	Mode of Exposure	Species/Strain/ Age/Weight	No. of Test Animals	No. of Controls	Duration and Frequency of Exposure	Total Length of Experiment	Effects	Reference and Rating
Acrolein 14 (6)	Inhalation chamber	Syrian golden hamsters, 100 ± 10 g	8 (M + F)	None	4 h	96 h; 1-2 animals sacrificed at 6 h, 12 h, 1 d, 2 d, and 4 d from the beginning of exposure	No recruitment of polymorphonuclear leukocytes to the epithelium of tracheas and intrapulmonary airways. Was cytotoxic: 50% of the ciliated cells exfoliated in the bronchi and cells of all airway surfaces were pale and swollen. Changes increased by 24 and 48 h (bleeding, cytoplasmic vacuoles, nuclear pallor, nuclear vacuoles, indented basal lamina), in both the trachea and bronchi. By 96 h there were areas of irregular epithelium with early stratification and hyperplasia, few ciliated cells, and reduced no. of cilia per cell.	Kilburn and McKenzie (1978) B-11
Acrolein < 14 (< 6) coated on carbon particles- 593 mg/m^3	Inhalation chamber	Syrian golden hamsters, 100 ± 10 g	10 (M + F)	None	4 h	8 d; 1-2 animals sacrificed at 6 h, 12 h, 1 d, 2 d, 4 d and 8 d from the beginning of the exposure	Caused leukocyte recruitment to the epithelium of tracheas and intrapulmonary airways, peaking at 12-24 h (carbon particles or acrolein alone caused no recruitment). No leukocytes were seen by day 8. Macrophages and unciliated epithelial cells in airway surfaces contained carbon particles.	Kilburn and McKenzie (1978) B-11

TABLE III-4. HAMSTERS--CHRONIC EXPERIMENTAL EXPOSURE TO ACROLEIN

Compound(s) and Concentration(s), mg/m^3 (ppm)	Humidity/ Temperature	Mode of Exposure	Species/Strain/ Age/Weight	No. of Test Animals	No. of Controls	Duration and Frequency of Exposure	Total Length of Experiment	Effects	Reference and Rating
Acrolein 11.4 (4.9)	23-24°C, 50-70%	Exposure chamber	Syrian golden hamsters, 10 wk, 88-124 g	20	20	6 h/d, 5 d/wk, 13 wk	13 wk	Closed eyes, salivation, and nasal discharge. 1 M died, of causes thought not to be treatment-related. Decreased food intake and body weight gain. Females showed significantly increased hematological values. Increased urinary sediments and decreased urinary crystals occurred. Increased organ-to-body weight ratios for lungs, heart, and kidneys. No effect on blood chemistry and histopathology of the lungs and bronchi. Histopathological changes were found in the epithelial lining of the nasal cavity, and the larynx of a few females. Focal hyper- and metaplasia of the tracheal epithelium in a few males and most females.	Feron et al. (1978) B-13
Acrolein 9.2 (4)		Cages suspended in inhalation chambers	Syrian golden hamsters (Mesocricetus auratus) 6 wk	18 M + 18 F exposed to acrolein only; 18 M 18 F exposed to acrolein and weekly intratracheal instillation of 0.9% NaCl	18 M + 18 F exposed to air only; 18 M + 18 F exposed to air and weekly intratracheal instillation of 0.9% NaCl	7 h/d, 5 d/wk, 52 wk	81 wk; 3 M + 3 F of each group were sacrificed at wk 52	There were no differences between the 2 exposure groups, so results were combined. Restless during wk 1. Closed eyes, salivation, and nasal discharge occurred for 1-2 wk, then disappeared. Slight decrease in body wt., the difference decreasing after exposure stopped. At wk 52, 8 controls and 2 test animals had died. By wk 80 a total of 23 controls and 20 test animals had died. Hematological and blood biochemical parameters unaffected. Inflammation and epithelial metaplasia of slight to moderate degree in the nasal cavity. 20% of the animals killed at wk 81 still showed treatment-related nasal cavity lesions. Changes in other parts of the respiratory tract. No respiratory tract tumors were found.	Feron and Kruysse (1977) B-13

(continued)

TABLE III-4. (concluded)

Compound(s) and Concentration(s), mg/m^3 (ppm)	Humidity/ Temperature	Mode of Exposure	Species/Strain/ Age/Weight	No. of Test Animals	No. of Controls	Duration and Frequency of Exposure	Total Length of Experiment	Effects	Reference and Rating
								A statistically insignificant increase in respiratory tract tumors was found in animals also exposed to low benzo(a)pyrene (18.2 mg total) compared to those exposed only to BP. In females, co-exposure to 36.4 mg BP caused increased tumors. Co-exposure to subcutaneously applied diethylnitrosamine caused no change in the incidence of respiratory tract tumors.	
Acrolein 3.3 (1.4)	23-24°C, 50-70%	Exposure chamber	Syrian golden hamsters, 10 wk, 88-124 g	20	20	6 h/d, 5 d/wk, 13 wk	13 wk	Sleeping and restlessness during exposure. No effect on growth, food intake, hematological values, blood chemistry, urinalysis, organ-to-body weight ratios, gross autopsy, and histopathology of the larynx, trachea, bronchi, and lungs. Minimal inflammatory changes were found in the nasal cavity.	Feron et al. (1978) B-13
Acrolein 0.93 (0.4)	23-24°C, 50-70%	Exposure chamber	Syrian golden hamsters, 10 wk, 88-124 g	20	20	6 h/d 5 d/wk, 13 wk	13 wk	No abnormal behavior. No changes in growth, food consumption, hematological values, blood chemistry, urinalysis, organ-to-body weight ratios, gross autopsy, or histopathology of the respiratory tract.	Feron et al. (1978) B-13

TABLE III-5. RATS--ACUTE EXPERIMENTAL EXPOSURE TO ACROLEIN

Compound(s) and Concentration(s), mg/m^3 (ppm)	Mode of Exposure	Species/Strain/ Age/Weight	No. of Test Animals	No. of Controls	Duration and Frequency of Exposure	Total Length of Experiment	Effects	Reference and Rating
Acrolein 100-5,000	Cylinder placed over mouth and nasal openings	Wistar rats, 250-450 g	56 M, for a total of of 111 exposures	Served as own controls	1 min at each of the levels tested		Significant changes in blood pressure (BP) and heart rate (HR) which began 15 s after exposure started, peaked at 30 s, and persisted until the end of exposure. Generally increased BP, but some decreases. Generally increased HR at the lower levels and decreased HR at higher levels. Overall, a pressor effect of increasing magnitude with increasing acrolein concentration. Rapid return to control levels in 10 s after exposure stopped. Pronounced cardioinhibitory effect was seen in the majority of animals at 2,500 and 5,000 mg/m^3.	Egle and Hudgins (1974) C-6
Acrolein 700	Inhalation chamber	White rats, 110-150 g	8		30 min	4 d	LD_{100}, deaths occurring up until the 4th day. Harked respiratory problems, animals gaping and jerking heads backward with each breath. Lacrimation, heavy secretion from the nose, and some rats had large frothy brown-colored bubbles in front of the nose. By the end, breathed with a snuffling sound and appeared listless. On autopsy: lung edema, hyperemia, and hemorrhages, degenerative changes in the bronchial epithelium, hyperemia of the heart, liver, and kidneys, and no changes in other organs.	Skog (1950) B-10
Acrolein 300	Inhalation chamber	White rats, 110-150 g			30 min	3 wk	LD_{50}, deaths occurring until the 4th day.	Skog (1950) B-10

(continued)

TABLE III-5. (continued)

Compound(s) and Concentration(s), mg/m^3 (ppm)	Mode of Exposure	Species/Strain/ Age/Weight	No. of Test Animals	No. of Controls	Duration and Frequency of Exposure	Total Length of Experiment	Effects	Reference and Rating
Acrolein 105-221 (45-95)	Inhalation chamber	Sprague-Dawley rats	7 M		30 min	14 d	The LC_{50} was in this range, no animals dying in 72 h after exposure to the low level and all the animals dying in the 72 h after exposure to the high level. Those surviving had no visible lesions when sacrificed 14 d post-exposure.	Potts et al. (1978) C-11
Acrolein 100	Inhalation chamber	White rats 110-150 g	8		30 min	3 wk	No mortality. Marked respiratory difficulty: gaping and jerking heads backward with each breath. Abundant lacrimation and heavy nasal secretion. By the end of the exposure, breathed with a snuffling sound and appeared listless. Majority recovered only after 4-5 d. On autopsy: lung edema, hyperemia, and hemorrhages, degenerative changes in the bronchial epithelium, hyperemia of the heart, liver, and kidneys, and no changes in other organs.	Skog (1950) B-10
Acrolein 50	Cylinder placed over mouth and nasal openings	Wistar rats, 250-450 g	9 M, for a total of 17 exposures	Served as own controls	1 min	2 min	Insignificant changes in blood pressure: 14/17 had a 20.4% increase, 3/17 had a 10.3% decrease. Significant changes in heart rate: 15/17 had a 7.5% increase, 2/17 had a 4.0% decrease.	Egle and Hudgins (1974) C-6

(continued)

TABLE III-5. (continued)

Compound(s) and Concentration(s), mg/m^3 (ppm)	Mode of Exposure	Species/Strain/ Age/Weight	No. of Test Animals	No. of Controls	Duration and Frequency of Exposure	Total Length of Experiment	Effects	Reference and Rating
Acrolein 46.6 (20)		Long-Evans rats	4	4	15 min		Caused a 40-50% decrease in respiration rate within 3 min; continuing throughout the exposure	Hartzell et al. (1976) C-7 Hartzell et al. (1977) C-8
Acrolein 46.6 (20) CO (3,700)		Long-Evans rats	4	4	~ 20 min		Compared to CO alone: a 40-50% decrease in respiration rate, extended the time to reach 60% carboxyhemoglobin in the blood by almost 40%, and increased the time to loss of avoidance response (incapacitation) by about 60%.	Hartzell et al. (1976) C-8 Hartzell et al. (1977) C-8
Acrolein 46.6 (20) CO (3,700) CO_2 (50,000)		Long-Evans rats	4	4	~ 20 min		Compared to CO alone or CO plus acrolein: increased respiration rate, decreased time to reach 60% carboxyhemoglobin in the blood, and decreased time to loss of avoidance response (incapacitation).	Hartzell et al. (1976) C-7 Hartzell et al. (1977) C-8
Acrolein 28 (12)	Inhalation chamber	Sprague-Dawley rats, "adult," 200-300 g	20 M	Controls used, but no. not given	4 h	52 h; 5 animals sacrificed at 0, 5, 24, and 48 h after exposure	During and following exposure: severe symptoms of eye and respiratory tract irritation, gasping and other signs of dyspnea, anorexia, and generalized weakness. Max. effects on enzyme activities were seen at 24 h, when the avg. alkaline phosphatase activities were 36% and 72% of control values for serum and lung, respectively.	Murphy et al. (1964) C-8
			Same age and weight					

(continued)

TABLE III-5. (continued)

Compound(s) and Concentration(s), mg/m^3 (ppm)	Mode of Exposure	Species/Strain/ Age/Weight	No. of Test Animals	No. of Controls	Duration and Frequency of Exposure	Total Length of Experiment	Effects	Reference and Rating
Acrolein 25	Cylinder placed over mouth and nasal openings	Wistar rats, 250-450 g	8 M, for a total of 25 exposures	Served as own controls	1 min	2 min	Insignificant changes: 20/25 had a 7.2% decrease in blood pressure, 15/25 had a 15.4% decrease in blood pressure, 25/25 had a 0.4% increase in heart rate.	Egle and Hudgins (1974) C-6
Acrolein 18.6 (8)	Inhalation chamber	Holtzman rats, 200-300 g	14 M; 6 were adrenal-ectomized	8 M; 4 were adrenal-ectomized	4 h	6 h	Increased liver enzyme (alkaline phosphatase and tyrosine transaminase) activity and slightly increased lung-to-body weight and liver-to-body weight ratios in intact animals. Adrenalectomized animals showed small increased in enzyme activities, increased lung-to-body weight ratio, and no change in liver-to-body weight ratio.	Murphy (1965) D-9
Acrolein 14.9 (6.4)	Inhalation chamber	Sprague-Dawley rats, "adult," 200-300 g	20 M Same age and weight; fasted 24 h before sacrifice	20? M	4 h	96 h; 5 animals sacrificed at 4, 24, 48, and 96 h after exposure	Liver alkaline phosphatase (AP) activity was significantly above control levels through 48 h post-exposure (a max. of ~ 325% at 24 h). Liver acetylcholine esterase activity was below controls for 48 h, significantly so only at 4 h (~ 80%). Liver/body weight ratio was significantly above that of controls at 24 h (~ 110%) and 48 h (~ 130%). Liver glutamic-oxaloacetic transaminase activity was increased, but not significantly. Mean adrenal weight was above controls (102-132%) for all post-exposure times, max. at 24 h. Avg. serum AP activity did not differ from controls. Lung AP activity was significantly decreased (36% lower) only at 4 h, probably due to dilution with edema fluid, because fresh lung/body weight ratio was 35% greater than controls.	Murphy et al. (1964) C-8

(continued)

TABLE III-5. (concluded)

Compound(s) and Concentration(s), mg/m^3 (ppm)	Mode of Exposure	Species/Strain/ Age/Weight	No. of Test Animals	No. of Controls	Duration and Frequency of Exposure	Total Length of Experiment	Effects	Reference and Rating
Acrolein 10.3 (4.4)	Inhalation chamber	Sprague-Dawley rats, "adult," 200-300 g	15 M	5 M	2-8 h Groups of 5 animals removed after 2-, 4-, or 8-h exposure; all sacrificed at 24 h	24 h	Lung and kidney alkaline phosphatase (AP) activity did not differ significantly from controls for any of the exposure groups. Those exposed for 2 h had liver AP activities 35% below controls but increasing exposure to 8 h increased liver AP to over twice control levels.	Murphy et al. (1964) C-8
Acrolein 10	Cylinder placed over mouth and nasal openings	Wistar rats, 250-450 g	8 M; for a total of 28 exposures	Served as own controls	1 min	2 min	Insignificant changes: 25/28 had an 8.5% increase in blood pressure, 3/28 had a 6.6% decrease in blood pressure, 28/28 had a 0.1% increase in heart rate.	Egle and Hudgins (1974) C-6
Acrolein 9.6 (4.1)	Inhalation chamber	Sprague-Dawley rats, "adult," 200-300 g	6 M	6 M	20 h	20 h	Liver/body weight ratio, weight of adrenals, and liver alkaline phosphatase (AP) activity all above control values. Lung and serum AP activity did not differ from controls. Lung/body weight ratio 14% greater than controls.	Murphy et al. (1964) C-8

TABLE III-6. RATS--REPEATED DOSE EXPERIMENTAL EXPOSURE TO ACROLEIN

Compound(s) and Concentration(s), mg/m³ (ppm)	Humidity/ Temperature	Mode of Exposure	Species/Strain/ Age/Weight	No. of Test Animals	No. of Controls	Duration and Frequency of Exposure	Total Length of Experiment	Effects	Reference and Rating
Acrolein 11.4 (4.9)	23-24°C, 50-70%	Exposure chamber	Wistar rats, specific pathogen free, 7 wk, 98-124 g	12	12	6 h/d, 5 d/wk, 13 wk	13 wk	Closed eyes and bristling hair during exposure. 3 M and 3 F died in the first 4 wk. Decreased food intake and body wt. gain. No effect on hematological values and blood chemistry. Increased urinary sediments and decreased urinary crystals. Increased relative wt. of lungs, heart, kidneys, and adrenals. Autopsy revealed hemorrhages and collapsed areas of the lungs, and chronic pleuritis in 1 M. Histopathological changes were found in the epithelial linings of the nasal cavity and larynx. Severe damage of the trachea, lungs, and bronchi were reported.	Feron et al. (1978) B-13
Acrolein 9.3 (4.0)		Inhalation chamber	Sprague-Dawley rats, "adult," 200-300 g	6 M	6 M	4 h/d, 5 d	5 d	Significantly lower liver/body wt. ratio (body wt. decreased 7% compared to a 3% increase in the controls). Lung, liver, and serum alkaline phosphatase activity, and lung and adrenal wt. did not differ from controls.	Murphy et al. (1964) C-8
Acrolein 9.1 (3.9)		Inhalation chamber	Sprague-Dawley rats, "adult," 200-300 g	6 M	6 M	4 h/d, 9 d	9 d	Significantly lower liver/body wt. radio (body wt. decreased 8% compared to a 3% increase in the controls). Lung, liver, and serum alkaline phosphatase activity and lung and adrenal wt. did not differ from controls.	Murphy et al. (1964) C-8

(continued)

TABLE III-6. (continued)

Compound(s) and Concentration(s), mg/m³ (ppm)	Humidity/ Temperature	Mode of Exposure	Species/Strain/ Age/Weight	No. of Test Animals	No. of Controls	Duration and Frequency of Exposure	Total Length of Experiment	Effects	Reference and Rating
Acrolein 8.6 ± 1.9 (3.7 ± 0.8)	77 ± 1°F, ~ 50%	Inhalation chamber	Sprague-Dawley rats	7 M 8 F	7 M 8 F	8 h/d, 5 d/wk, 6 wk	6 wk	No effect on behavior, hematological values, and various liver and serum enzyme activities. Rate of body wt. gain was significantly less than that of the controls for both males and females. Nonspecific inflammatory changes in the lungs, liver, and kidneys. Focal calcification of renal tubular epithelium.	Lyon et al. (1970) B-12
Acrolein 4.9 (2.1)		Inhalation chamber	Sprague-Dawley rats, "adult," 200-300 g	12 M	12 M	41 h	41 h	Liver/body weight ratio, adrenal weight, and liver alkaline phosphatase (AP) activity were all significantly above controls. Lung and serum AP activity and lung weight did not differ from controls.	Murphy et al. (1964) C-8
Acrolein 4.2 (1.8)	77 ± 1°F, ~ 50%	Inhalation chamber	Sprague-Dawley rats	7 M 8 F	7 M 8 F	90 d	90 d	No effect on behavior or hematological values. Rate of wt. gain was significantly lower than that of the controls with equivalent starting wts. Nonspecific inflammatory changes in brain, heart, lung, liver, and kidney.	Lyon et al. (1970) B-12

(continued)

TABLE III-6. (continued)

Compound(s) and Concentration(s), mg/m³ (ppm)	Humidity/ Temperature	Mode of Exposure	Species/Strain/ Age/Weight	No. of Test Animals	No. of Controls	Duration and Frequency of Exposure	Total Length of Experiment	Effects	Reference and Rating
Acrolein 3.3 (1.4)	23-24°C, 50-70%	Exposure chamber	Wistar rats, specific pathogen free, 7 wk, 98-124 g	12	12	6 h/d, 5 d/wk, 13 wk	13 wk	At each exposure there was initial hyperactivity followed by restless sleep. Decreased food intake and body weight gain. No effect on hematological values, blood chemistry, urinalysis, organ-to-body wt. ratios, gross autopsy, or histopahology of the larynx, trachea, bronchi, and lungs. Squamous metaplasia and neutrophilic infiltration of the mucosa were found in the nasal cavity.	Feron et al. (1978) B-13
Acrolein 2.3 (1.0)	77 ± 1°F, ~ 50%	Inhalation chamber	Sprague-Dawley rats	7 M 8 F	7 M 8 F	90 d	90 d	No effect on behavior or hematological values. Some showed focal liver necrosis (minute foci without any specific pattern) and occasional pulmonary hemorrhage. Rate of wt. gain was significantly lower than that of controls with equivalent starting wts.	Lyon et al. (1970) B-12
Acrolein 2.3 (1.0)		Inhalation chamber	Sprague-Dawley rats, "adult," 200-300 g	12 M	12 M	81 h	81 h	Liver/body wt. ratio, adrenal wt., lung wt., and liver, lung, and serum alkaline phosphatase activity did not differ from control values.	Murphy et al. (1964) C-8

(continued)

TABLE III-6. (continued)

Compound(s) and Concentration(s), mg/m^3 (ppm)	Humidity/ Temperature	Mode of Exposure	Species/Strain/ Age/Weight	No. of Test Animals	No. of Controls	Duration and Frequency of Exposure	Total Length of Experiment	Effects	Reference and Rating
Acrolein 1.6 ± 0.2 (0.7 ± 0.1)	77 ± 1°F ~ 50%	Inhalation chamber	Sprague-Dawley rats	7 M 8 F	7 M 8 F	8 h/d, 5 d/wk, 6 wk	6 wk	No effect on behavior, body wt. gain, hematological values, and various serum and liver enzyme activities. Lungs showed mild chronic inflammatory changes and occasional emphysema. No definite alteration of the respiratory epithelium or peribronchial smooth musculature.	Lyon et al. (1970) B-12

(continued)

TABLE III-6. (continued)

Compound(s) and Concentration(s), mg/m^3 (ppm)	Humidity/ Temperature	Mode of Exposure	Species/Strain/ Age/Weight	No. of Test Animals	No. of Controls	Duration and Frequency of Exposure	Total Length of Experiment	Effects	Reference and Rating
Acrolein 1.52 ± 0.05		Inhalation chamber	White rats	10 M	10 M	24 d	101 d (with a 21-d pre- and a 56-d post-exposure period)	By 10 d of exposure all were sluggish and apathetic, their coats lost luster, and they had poor appetites. There was progressive deterioration in their general condition. 7/10 died. Wt. loss up to 14% by 24 d. Changes in the magnitude of conditioned motor response (decreased response to a bell) and the latent period of the response (increase in response to light) began at 10 d, and continued throughout exposure. An insignificant increase in urine coproporphyrin levels during exposure, a significant decrease by 5 wk post-exposure, and back to control levels by 8-wk recovery. Blood cholinesterase activity significantly decreased by wk 2, and returned to normal only 20 d post-exposure. Statistically significant increase in fluorescent leucocyte count after 1 wk, continuing throughout exposure, and began to decrease towards normal at 11 d post-exposure. On autopsy, the lungs showed drastic changes of an inflammatory nature. Myocardium and liver showed marked changes (granular and fatty dystrophy, and necrosis).	Gusev et al. (1966) B-9

(continued)

TABLE III-6. (continued)

Compound(s) and Concentration(s), mg/m³ (ppm)	Humidity/ Temperature	Mode of Exposure	Species/Strain/ Age/Weight	No. of Test Animals	No. of Controls	Duration and Frequency of Exposure	Total Length of Experiment	Effects	Reference and Rating
Acrolein 1.24 - 1.31 (0.53-0.56)	21°C, 58%	Inhalation chamber	OFA rats, specific pathogen free	163 M Same age and avg. weight	163 M	15, 32, or 77 d	77 d	The ratio of the weight of the lungs to the body weight was significantly above that of the controls only on day 77. The ratio of the weight of the liver to body wt. was significantly below that of the controls on day 15, but there was no difference on days 32 or 77. There were no differences in levels of serum alkaline phosphatase or liver alcohol dehydrogenase and oxidation reduction enzymes on any days. Serum acid phosphatase level was below that of the controls only on day 15.	Bouley et al. (1975) B-10 Bouley et al. (1976) B-10
Acrolein 1.24-1.31 (0.53-0.56)	21°C, 58%	Inhalation chamber	OFA rats, specific pathogen free	20 M Same age and avg. weight	20 M	21 d	60 d	Sneezing occurred between days 7 and 21. Body weight was significantly less than control value during exposure and after. The difference began decreasing after the exposure stopped and ceased to be significant by day 60. Food consumption was significantly less than that of the controls during exposure, and above that of the controls after the exposure stopped.	Bouley et al. (1975) B-10 Bouley et al. (1976) B-10
Acrolein 1.24-1.31 (0.53-0.56)	21°C, 58%	Inhalation chamber	OFA rats, specific pathogen free	25 M Same age and avg. weight	25 M	60 d	60 d	Sneezing during days 7-21, then it stopped. Body weight was significantly below that of the controls after day 7.	Bouley et al. (1975) B-10 Bouley et al. (1976) B-10

(continued)

TABLE III-6. (continued)

Compound(s) and Concentration(s), mg/m³ (ppm)	Humidity/ Temperature	Mode of Exposure	Species/Strain/ Age/Weight	No. of Test Animals	No. of Controls	Duration and Frequency of Exposure	Total Length of Experiment	Effects	Reference and Rating
Acrolein 1.24-1.31 (0.53-0.56)	21°C, 58%	Inhalation chamber	OFA rats, specific pathogen free	3 M, 21 F Same age and avg. weight	3 M, 21 F	26 d	26 d	No differences in number of pregnant rats, or number and avg. weight of fetuses.	Bouley et al. (1975) B-10 Bouley et al. (1976) B-10
Acrolein 1.24-1.31 (0.53-0.56) Followed by exposure to an aerosol of *S. enteritidis* 1×10^6/rat (~ LD_{50})	21°C, 58%	Inhalation chamber	OFA rats, specific pathogen free	32 M Same age and avg. weight. Both received bacterial dose	31 M	18 or 63 d	63+ d	When the bacterial dose was given after 18 d of acrolein exposure, there was a significant increase in mortality (15/16) compared to controls (8/15). When given after 63 d of gas exposure, there was no difference (10/16).	Bouley et al. (1975) B-10 Bouley et al. (1976) B-10
The thermal decomposition products of low density polyethylene: Acrolein 1.11 ± 0.30 (avg. 0.48 ± 0.12) HCHO 1.70 ± 0.25 (avg. 1.36 ± 0.20) Total aldehydes (17 7 ± 0.6) CO (≤ 20) Particulates 8.0 ± 0.6		Inhalation chamber	Wistar rats, 240 ± 22 g	15 M	9 M	6 h/night, 5 night/wk, 2-5 wk	5 wk; 5 animals sacrificed at 2, 3, and 5 wk	Animals conspicuously inactive during exposure periods, and were not easily alerted. Increased preening during non-exposure periods. Brain glutathione levels and lysosomal acid proteinase activity were unaffected. Brain RNA levels were above controls at wk 2 and 5. Microsomal superoxide dismutase was above control levels at wk 5. Glycosylation of cerebral protein molecules *in vitro* was more rapid at wk 2, then decreasing to near control levels. Cytosolic NADPH (reduced nicotinamide-adenine dinucleotide phosphate) diaphorase activity in the brain was below control levels at wks 2, 3, and 5.	Zitting and Savolainen (1979) C-10

(continued)

TABLE III-6. (continued)

Compound(s) and Concentration(s), mg/m^3 (ppm)	Humidity/ Temperature	Mode of Exposure	Species/Strain/ Age/Weight	No. of Test Animals	No. of Controls	Duration and Frequency of Exposure	Total Length of Experiment	Effects	Reference and Rating
Acrolein 0.74 ± 0.13			Albino rats	10 healthy M, 10 M with experimentally induced silicosis	10 healthy M, 10 M with experimentally induced silicosis	61 d, with starvation during the last 10 d	61+ d	General state and weight was significantly affected by the 5th wk for the "sick" animals and by the 6th wk for the "healthy" animals. Changes in the chronaxy of the antagonistic muscles in both groups. Change in blood cholinesterase activity before starvation in the "sick" rats, but became significant only after starvation in the "healthy" rats. Recovery was slower in the "sick" animals. Increase in 17-ketosteroids in the urine in both groups, greater in "sick" rats. Vitamin C levels in the adrenals decreased somewhat in "healthy" animals, and was statistically significant in the "sick" ones.	Sinkuvene (1970) B-8
Acrolein 0.51 (0.22)	77 ± 1°F, ~ 50%	Inhalation chamber	Sprague-Dawley rats	15 M 15 F	15 M 15 F	90 d	90 d	No effect on behavior, wt. gain, or hematological values. Apparently no changes found on autopsy.	Lyon et al. (1970) B-12

(continued)

TABLE III-6. (continued)

Compound(s) and Concentration(s), mg/m^3 (ppm)	Humidity/ Temperature	Mode of Exposure	Species/Strain/ Age/Weight	No. of Test Animals	No. of Controls	Duration and Frequency of Exposure	Total Length of Experiment	Effects	Reference and Rating
Acrolein 0.51 ± 0.02		Inhalation chamber	White rats, 90-130 g	10 M	10 M	61 d	103 d (with 21-d pre- and post-exposure periods)	No changes in the behavior and general condition. Lost wt. Loss of conditioned reflexes after 10 d of exposure, followed by disturbance of spatial relationships (which is dependent on cortical activity), both of which returned to normal after exposure stopped. Urine coproporphyrin levels significantly decreased, especially at wk 7, then returned to normal during recovery. Blood cholinesterase activity decreased, becoming significant from 34-41 d, then began to increase, reaching normal levels by 10 d post-exposure. Fluorescent leucocyte counts began increasing at wk 1, and continued until 11 d of recovery, when it began to decrease to normal. On autopsy: proliferation of the columnar epithelium of the bronchi with excess production of mucus, and marked eosinophilic infiltration of the bronchial wall.	Gusev et al. (1966) B-9
Acrolein 0.15 ± 0.01		Inhalation chamber	White rats, 90-130 g	10 M	10 M	61 d	103 d (with 21-d pre- and post-exposure periods)	No changes in: behavior, general condition, wt., magnitude or latent period of conditioned motor reflexes, urine coproporphyrin levels, or blood cholinesterase activity. An increase (of little toxicological significance) in fluorescent leukocyte counts after 24 h of exposure. No appreciable changes found on autopsy.	Gusev et al. (1966) B-9

(continued)

TABLE III-6. (concluded)

Compound(s) and Concentration(s), mg/m^3 (ppm)	Humidity/ Temperature	Mode of Exposure	Species/Strain/ Age/Weight	No. of Test Animals	No. of Controls	Duration and Frequency of Exposure	Total Length of Experiment	Effects	Reference and Rating
Acrolein 0.14 ± 0.029			Albino rats	10 healthy M, 10 M with experimentally induced silicosis	10 healthy M, 10 M with experimentally induced silicosis	61 d with starvation during the last 10 d	61+ d	"Sick" rats displayed statistically significant changes in the chronaxy of antagonistic muscles and in the vitamin C content of the adrenals. Changes were produced in the "healthy" rats (details not given).	Sinkuvene (1970) B-8
Acrolein 0.03 ± 0.015			Albino rats	10 healthy M, 10 M with experimentally induced silicosis	10 healthy M, 10 M with experimentally induced silicosis	61 d, with starvation during the last 10 d	61+ d	No changes in a variety of biological, biochemical, and physiological tests in either the "sick" or the "healthy" animals. This level was recommended as the one-time maximum permissible concentration and the mean diurnal maximum permissible concentration.	Sinkuvene (1970) B-8

TABLE III-7. RATS--CHRONIC EXPERIMENTAL EXPOSURE TO ACROLEIN

Compound(s) and Concentration(s), mg/m³ (ppm)	Humidity/ Temperature	Mode of Exposure	Species/Strain/ Age/Weight	No. of Test Animals	No. of Controls	Duration and Frequency of Exposure	Total Length of Experiment	Effects	Reference and Rating
Acrolein 4.7 (2) During days 61 to 63, exposure slowly increased to 12 mg/m³, remained at that level for ~ 15 h, then slowly decreased		Inhalation chamber	Albino, Sprague-Dawley Souche OFA rats, specific pathogen free, 3 mo, ~ 175 g	50 M For each lot: 2 used for ventilation resistance measurements; 3 for hematology; 4 for urinary vanillyl-mandelic acid (VMA) levels; 2 for pulmonary surfactant measurements	50 M	91 d; groups of 6 sacrificed on days 7, 14, 35, and 90 of exposure for respiratory tract histopathology	105 d	One rat died following the accident. Decreased wt. gain before the accident, slight wt. decrease for ~ 3 wk following the accident, then decreased wt. gain. After 2 wk of recovery, body wt. (~ 375 g) still below that of the controls (~ 525 g) and 2.3 mg/m³ group (~ 425 g). Slight changes in ventilatory resistance. No significant changes in hematological values (cell counts, hematocrit, leukocytes, mean cell volume, and hemoglobin level) at any time. Decreased VMA levels after wk 2 to the end of exposure. The index of stability of pulmonary surfactant was decreased on day 7, the difference smaller on day 28, and normal by day 91. Loss of cilia in the bronchi during 1st 5 wk, then normal. Perivascular edema was seen from day 35 to day 90. On days 7 to 35, no change in the surface of the alveoli, no cellular proliferation, no exudates, and no abnormal levels of macrophages.	Guillerm et al. (1974) C-12

(continued)

TABLE III-7. (continued)

Compound(s) and Concentration(s), mg/m^3 (ppm)	Humidity/ Temperature	Mode of Exposure	Species/Strain/ Age/Weight	No. of Test Animals	No. of Controls	Duration and Frequency of Exposure	Total Length of Experiment	Effects	Reference and Rating
Acrolein 2.3 (1) Accidentally exposed to ~ 21 mg/m^3 for ~ 18 h on day 29, then to 0 mg/m^3 for ~ 12 h		Inhalation chamber	Albino, Sprague-Dawley Souche OFA rats, specific pathogen free, 3 mo, ~ 175 g	50 M For each lot: 2 used for ventilation resistance measurements; 3 for hematology; 4 for urinary vanillylmandelic acid (VMA); and 2 for pulmonary surfactant measurements	50 M	91 d; groups of 6 sacrificed on days 7, 14, 35, and 90 of exposure for respiratory tract histopathology	105 d	15 rats died in the 9 d following the accident. Wt. increase significantly below controls, even before the accidental exposure, which caused a sharp wt. loss of ~ 25 g. By 2 wk of recovery, wt. still below controls (~ 425 g vs. ~ 525 g). Increased expiration resistance only on day 22. No difference in resistance (inspiration and expiration) any other day, before or after accident. No significant changes in hematological values (hematocrit, cell counts, leukocytes, mean cell volume, and hemoglobin levels) at any time. Changes in VMA (vanillylmandelic acid) levels (nonspecific indication of stress), generally reduced by day 70. In the 1st wk, a decrease in the index of stability of the pulmonary surfactant, the difference smaller by day 28, and normal by day 91. Slight loss of ciliation in the bronchi by 7 d, increasing on days 14 and 35, normal after that. Perivascular edema was seen after day 35. On days 7-35, no change in the surface of the alveoli, no cellular proliferation, no exudates, and no abnormal levels of macrophages.	Guillerm et al. (1974) C-12

(continued)

TABLE III-7. (concluded)

Compound(s) and Concentration(s), mg/m³ (ppm)	Humidity/ Temperature	Mode of Exposure	Species/Strain/ Age/Weight	No. of Test Animals	No. of Controls	Duration and Frequency of Exposure	Total Length of Experiment	Effects	Reference and Rating
Acrolein 1.23-1.47 (0.53-0.63)	56% 20°C	Inhalation chamber, 0.3 m³, air flow 5 m³/h	Sprague-Dawley rats, specific pathogen free	30 M Same age and avg. weight. Only 15 of each group actually examined for changes.	30 M	2-6 mo	6 mo	Avg. body weight significantly below controls after day 13, accompanied by decreased food and water consumption. Significantly decreased avg. lung weight, perhaps due to different body development and the lower body weight. No differences in number or activity of alveolar macrophages. Bronchial ciliated epithelium unchanged. Alveolar changes: thickening, indicating reticular hypertrophy; and thinning, as in emphysema. Cell damage in the liver. No damage to kidneys, spleen, stomach, and heart.	Roussel et al. (1973) B-9
Acrolein 1.24-1.31 (0.53-0.56)	21°C 58%	Inhalation chamber	OFA rats, specific pathogen free	10 M Same age and avg. weight	10 M	10-180 d	180 d	After 10-26 d of exposure, the number of alveolar macrophages recovered by lavage was below that of the controls. There were no differences in relative numbers of cells, viability during lavage, and physiological activity. After 60-180 d of exposure, there were no significant differences.	Bouley et al. (1975) B-10; Bouley et al. (1976) B-10
Acrolein 0.93 (0.4)	23-24°C, 50-70%	Exposure chamber	Wistar rats, specific pathogen free, 7 wk, 98-124 g	12	12	6 h/d, 5 d/wk, 13 wk	13 wk	No abnormal behavior. Slight, consistent, but statistically insignificant, growth retardation. No effect on food intake, hematological values, serum enzyme activities, urinalysis, organ-to-body weight ratios, gross autopsy, and histopathology of the tracheas, bronchi, and lungs. 1 M rat showed metaplastic and inflammatory changes in the nasal cavity.	Feron et al. (1978) B-13

TABLE III-8. GUINEA PIGS--ACUTE EXPERIMENTAL EXPOSURE TO ACROLEIN

Compound(s) and Concentration(s), mg/m^3 (ppm)	Mode of Exposure	Species/Strain/ Age/Weight	No. of Test Animals	No. of Controls	Duration and Frequency of Exposure	Total Length of Experiment	Effects	Reference and Rating
Acrolein 3,728 (1,600)	Tracheotomy	Guinea pigs, ~ 250 g			6 min	6 min	Dead in ~ 6 min without any measurable increase in pulmonary resistance.	Davis et al. (1967) C-6
Acrolein 932 (400)	Inhalation	Guinea pigs, ~ 250 g			60 min?	60+ min?	Full recovery within 5 min after the end of exposure. Duration of exposure unclear, and symptoms not given.	Davis et al. (1967) C-6
Acrolein 39.6 (17)	Tracheotomy	Guinea pigs, ~ 250 g	6	Served as own controls	60 min	60 min	No change in respiratory resistance, rate, or minute volume.	Davis et al. (1965) C-5 Davis et al. (1967) C-6
Acrolein 39.6 (17)	Inhalation	Guinea pigs, ~ 250 g	6	Served as own controls	60 min	60 min	Significantly increased pulmonary resistance and decreased respiratory rate. No change in minute volume according to the 1965 report, but a significant decrease in minute volume according to the 1967 report. No change in compliance. Authors conclude that these responses (see results of other entries for Davis et al., 1965, 1967) indicate stimulation of receptors in the supraglottal passages causing reflex respiratory changes.	Davis et al. (1965) C-5 Davis et al. (1967) C-6

(continued)

TABLE III-8. (concluded)

Compound(s) and Concentration(s), mg/m³ (ppm)	Mode of Exposure	Species/Strain/ Age/Weight	No. of Test Animals	No. of Controls	Duration and Frequency of Exposure	Total Length of Experiment	Effects	Reference and Rating
Acrolein 2.3 (1.0)	Face masks	Random-bred guinea pigs, 300-400 g	10 M	Served as own controls	2 h	3-3.5 h (includes a 1-1.5 h pre-exposure period)	Tidal volume and total respiratory flow resistance during expiration and inspiration increased significantly and respiratory rate decreased. All changes greater than those for exposure to 0.6, 0.4, and 0.2 ppm.	Murphy et al. (1963) B-10
Acrolein 1.4 (0.6)	Face masks	Random-bred guinea pigs, 300-400 g	10 M	14 M during expt., and own pre-exposure values	2 h	~ 4.5 h (a 1 h pre- and 1.5 h post-exposure period)	Increased expiratory flow resistance and tidal volume and decreased respiration rate throughout exposure. Responses were rapid, reaching max. in 30-60 min and then remaining constant. After exposure stopped, rapid return to pre-exposure and control values. Changes greater than those for 0.2 and 0.4 ppm.	Murphy et al. (1963) B-10
Acrolein ~ 0.9 (~ 0.4)	Face mask	Random-bred guinea pigs, 300-400 g	15 M	Served as own controls	2 h	3-3.5 h (includes a 1-1.5 h pre-exposure period)	Significantly increased total respiratory resistance during inspiration and expiration. Respiratory rate decreased. Changes greater than those for 0.2 ppm.	Murphy et al. (1963) B-10
Acrolein 0.47 (0.2)	Face masks	Random-bred guinea pigs, 300-400 g	5 M	Served as own controls	2 h	3-3.5 h (includes a 1-1.5 h pre-exposure period)	Slight increase in total respiratory flow resistance during expiration and inspiration. Slight decreases in respiratory rate and minute volume. No change in tidal volume.	Murphy et al. (1963) B-10

TABLE III-9. GUINEA PIGS--REPEATED DOSE EXPERIMENTAL EXPOSURE TO ACROLEIN

Compound(s) and Concentration(s), mg/m^3 (ppm)	Humidity/ Temperature	Mode of Exposure	Species/Strain/ Age/Weight	No. of Test Animals	No. of Controls	Duration and Frequency of Exposure	Total Length of Experiment	Effects	Reference and Rating
Acrolein 8.6 ± 1.9 (3.7 ± 0.8)	77 ± 1°F, ~ 50%	Inhalation chamber	Princeton or Hartley guinea pigs	7 M 8 F	7 M 8 F	8 h/d, 5 d/wk, 6 wk	6 wk	No effect on behavior, hematological values, or various serum and liver enzyme activities. Lower rate of body weight gain. Non-specific inflammatory changes in lungs, livers, and kidneys.	Lyon et al. (1970) B-12
Acrolein 4.2 (1.8)	77 ± 1°F, ~ 50%	Inhalation chamber	Princeton or Hartley guinea pigs	6 M 9 F	6 M 9 F	90 d	90 d	No effect on behavior, weight gain, or hematological values. Non-specific inflammatory changes in the brain, heart, lung, liver, and kidney.	Lyon et al. (1970) B-12
Acrolein 2.3 (1.0)	77 ± 1°F, ~ 50%	Inhalation chamber	Princeton or Hartley guinea pigs	7 M 8 F	7 M 8 F	90 d	90 d	No effect on behavior, weight gain, or hematological values. Various degrees of pulmonary inflammation and occasional minute foci of liver necrosis without any specific pattern.	Lyon et al. (1970) B-12
Acrolein 1.6 ± 0.2 (0.7 ± 0.1)	77 ± 1°F, ~ 50%	Inhalation chamber	Princeton or Hartley guinea pigs	7 M 8 F	7 M 8 F	8 h/d, 5 d/wk, 6 wk	6 wk	No effect on behavior, body weight gain, hematological values, or various serum and liver enzyme activities. Lungs showed mild chronic inflammatory changes and occasional emphysema. No definite alteration of the respiratory epithelium or of the peribronchial smooth musculature.	Lyon et al. (1970) B-12
Acrolein 0.51 (0.22)	77 ± 1°F, ~ 50%	Inhalation chamber	Princeton or Hartley guinea pigs	15 M 15 F	15 M 15 F	90 d	90 d	No effect on behavior, weight gain, or hematological values. Non-specific inflammatory changes in liver, lung, kidney, and heart.	Lyon et al. (1970) B-12

TABLE III-10. CHICKENS--REPEATED DOSE EXPERIMENTAL EXPOSURE TO ACROLEIN

Compound(s) and Concentration(s), mg/m^3 (ppm)	Mode of Exposure	Species/Strain/ Age/Weight	No. of Test Animals	No. of Controls	Duration and Frequency of Exposure	Total Length of Experiment	Effects	Reference and Rating
Acrolein 466 (200)	Endo-tracheal cannulae attached to a vapor chamber	White leghorn chickens, 1.3-1.8 kg	30 F	12 F	5 min/d, for up to 27 d	27 d, animals sacrificed on days 1, 3, 6, 13, 20, and 27	First signs of toxicity occurred on day 6: reduction in percent ciliation and number of mucus glands. The number of goblet cells began decreasing on day 13. All continued to decline, the mucus elements most severely. The inflammatory response was localized in the mucosa and lamina propria, began day 1, was manifested mainly by a lymphocytic infiltrate, and increased with time. The symptoms were more severe in the upper than the lower trachea.	Denine (1971) C-12
Acrolein 116.5 (50)	Endo-tracheal cannulae attached to a vapor chamber	White leghorn chickens, 1.3-1.8 kg	10 F	10F	5 min/d, for 13 or 17 d	17 d	Upper trachea: slight decreases in percent ciliation on days 13 and 17. Decreased number of mucus glands on day 13, but no further change. Number of goblet cells markedly decreased on both days. Changes are less severe than those caused by 200 ppm after the same length of time. Lower trachea: no effect on percent ciliation. Slight decrease in number of goblet cells. Slight increase in mucus glands.	Denine (1971) C-12

TABLE III-11. RABBITS--ACUTE EXPERIMENTAL EXPOSURE TO ACROLEIN

Compound(s) and Concentration(s), mg/m^3 (ppm)	Mode of Exposure	Species/Strain/ Age/Weight	No. of Test Animals	No. of Controls	Duration and Frequency of Exposure	Total Length of Experiment	Effects	Reference and Rating
Acrolein 28 (12)	Inhalation (perhaps head exposure only)	Rabbits, anesthetized with urethane	50		Probably ~ 5 min (text unclear)		Decreased heart rate, increased arterial pressure, and inhibition of respiratory movements.	Kishi et al. (1975) C-8
Acrolein 21 (9)	Inhalation (perhaps head exposure only)	Rabbits			Probably ~ 5 min (text unclear)		Slight decrease in heart rate towards the end of the exposure, of dubious importance. No change in arterial pressure or respiratory movement.	Kishi et al. (1975) C-8

TABLE III-12. RABBITS--CHRONIC EXPERIMENTAL EXPOSURE TO ACROLEIN

Compound(s) and Concentration(s), mg/m^3 (ppm)	Humidity/ Temperature	Mode of Exposure	Species/Strain/ Age/Weight	No. of Test Animals	No. of Controls	Duration and Frequency of Exposure	Total Length of Experiment	Effects	Reference and Rating
Acrolein 11.4 (4.9)	23-24°C, 50-70%	Exposure chamber	Dutch rabbits, 6-9 wk, 0.66 - 1.22 kg	4	4	6 h/d, 5 d/wk, 13 wk	13 wk	Closed eyes, sneezing, and occasional breathing difficulty during exposure. Decreased food intake and body weight gain. Increased relative weight of the lungs. Increased urinary sediments. No effect on hematological values, blood chemistry, gross autopsy, and histopathology of the larynx. Histopathological changes were seen in the epithelial lining of the nasal cavity, trachea, bronchi, and lungs.	Feron et al. (1978) B-13
Acrolein 3.3 (1.4)	23-24°C, 50-70%	Exposure chamber	Dutch rabbits, 6-9 wk, 0.66-1.22 kg	4	4	6 h/d, 5 d/wk, 13 wk	13 wk	Occasional sneezing. Decreased food intake and body weight gain. No effect on hematological values, blood chemistry, urinalysis, organ-to-body weight ratios, gross autopsy, or histopathology of the respiratory tract.	Feron et al. (1978) B-13
Acrolein 0.93 (0.4)	23-24°C, 50-70%	Exposure chamber	Dutch rabbits, 6-9 wk, 0.66 - 1.22 kg	4	4	6 h/d, 5 d/wk, 13 wk	13 wk	No abnormal behavior. 1 F control and 1 M test animal died. No effect on growth, food intake, hematological values, blood chemistry, urinalysis, organ-to-body weight ratios, gross autopsy, or histopathology of the respiratory tract.	Feron et al. (1978) B-13

TABLE III-13. CATS--ACUTE EXPERIMENTAL EXPOSURE TO ACROLEIN

Compound(s) and Concentration(s), mg/m^3 (ppm)	Mode of Exposure	Species/Strain/ Age/Weight	No. of Test Animals	No. of Controls	Duration and Frequency of Exposure	Total Length of Experiment	Effects	Reference and Rating
Acrolein avg. 210 range 180-240	Inhalation	Cat, 1,750 g	1		2 h 40 min; 1st h at 240 mg/m^3, later at 180 mg/m^3	Few days	Immediately: tearing, first thinly then thickly flowing salivary secretion, coughing, sneezing. After 10 min: respiration 12-16 interrupted by swallowing, open mouth, tongue outstretched, continuous salivation. After 40 min: coughing, head on neck, jerky respiration 20. After 80 min: head moved with each inspiration, clearly dyspneic. After 85 min: spasmodic sneezing, choking, strong dyspnea.	Iwanoff (1911) C-8
Acrolein avg. 40 range 34-46	Inhalation	Cat, 2,400 g	1		4 h; 1st 2.5 h at 34 mg/m^3, later at 46 mg/m^3	Several days	Immediately: tearing, salivation, sneezing. After 10 min: nasal secretions, eyes closed, respiration 16. 15-150 min: slight retching motions without vomiting, copious salivation, respiratory 18-20 through wide open mouth. After 160 min: frequent retching, no vomiting, some dyspnea, nasal and salivary secretions. After exposure: remained sick for several days, but it recovered.	Iwanoff (1911) C-8
Acrolein avg. 25 range 20-30	Inhalation	Cat, 2,000 g	1		9 h 40 min; 1st 2 h at 27 mg/m^3, next 4 h at 30 mg/m^3, later at 20 mg/m^3	10+ h	First 105 min: quiet, respiration 14-16, copious salivation, eyes closed. After 155 min: head down towards neck, eyes closed, sleepy. After 305 min: light retching motions. Toward the end: quiet, in a half slumber, respiration 16. After exposure: appeared to be entirely normal after "several hours."	Iwanoff (1911) C-8

(continued)

TABLE III-13. (concluded)

Compound(s) and Concentration(s), mg/m^3 (ppm)	Mode of Exposure	Species/Strain/ Age/Weight	No. of Test Animals	No. of Controls	Duration and Frequency of Exposure	Total Length of Experiment	Effects	Reference and Rating
Acrolein avg. 25 range 23-27	Inhalation	Cats, 2,000 g	1		3.5 h; 1st 2 h at 27 mg/m^3 later at 23 mg/m^3	3.5+ h	Immediately: tearing, viscous salivary secretions, leaking, sneezing. After 135 min: respiration 19, occasional salivation, eyes closed, breathing through mouth, quiet, sleepy, head on neck. After exposure: appeared to be normal "after a short time."	Iwanoff (1911) C-8

TABLE III-14. MONKEYS--REPEATED DOSE EXPERIMENTAL EXPOSURE TO ACROLEIN

Compound(s) and Concentration(s), mg/m³ (ppm)	Humidity/ Temperature	Mode of Exposure	Species/Strain/ Age/Weight	No. of Test Animals	No. of Controls	Duration and Frequency of Exposure	Total Length of Experiment	Effects	Reference and Rating
Acrolein 8.6 ± 1.9 (3.7 ± 0.8)	77 ± 1°F, ~ 50%	Inhalation chamber	Squirrel monkeys (Saimiri sciurea)	9 M	9 M	8 h/d, 5 d/wk, 6 wk	6 wk	During the 1st week of exposure, salivated excessively, blinked frequently, and kept their eyes closed. Symptoms were milder the 2nd wk. 1 died on d 6, and 1 on d 9. Decreased rate of body wt. gain. No effect on hematological values or various serum and liver enzyme activities. Nonspecific inflammatory changes in lung, liver, and kidney. Focal calcification of renal tubular epithelium. Squamous metaplasia and basal cell hyperplasia of the trachea. Necrotizing bronchitis and bronchiolitis with squamous metaplasia of the lungs.	Lyon et al. (1970) B-12
Acrolein 4.2 (1.8)	77 ± 1°F, ~ 50%	Inhalation chamber	Squirrel monkeys (Saimiri sciurea)	9 M	9 M	90 d	90 d	Excessive salivation and ocular discharge. No effect on wt. gain or hematological values. Nonspecific inflammatory changes in the brain, heart, lung, liver, and kidney. All showed squamous metaplasia and 6/9 showed basal cell metaplasia of the trachea.	Lyon et al. (1970) B-12
Acrolein 2.3 (1.0)	77 ± 1°F, ~ 50%	Inhalation chamber	Squirrel monkeys (Saimiri sciurea)	9 M	9 M	90 d	90 d	Ocular and nasal discharge throughout exposure, decreasing in severity. Kept eyes closed for extended periods. 1 died on day 28, probably due to infection from a bite. No effect on wt. gain or hematological values. Parasitic infection in some with involvement of the lung, liver, heart, and brain.	Lyon et al. (1970) B-12

(continued)

TABLE III-14. (concluded)

Compound(s) and Concentration(s), mg/m³ (ppm)	Humidity/ Temperature	Mode of Exposure	Species/Strain/ Age/Weight	No. of Test Animals	No. of Controls	Duration and Frequency of Exposure	Total Length of Experiment	Effects	Reference and Rating
Acrolein 1.6 ± 0.2 (0.7 ± 0.1)	77 ± 1°F, ~ 50%	Inhalation chamber	Squirrel monkeys (Saimiri sciurea)	9 M	9 M	8 h/d, 5 d/wk, 6 wk	6 wk	No effect on behavior, body wt. gain, hematological values, or various serum and liver enzyme activities. Lungs showed chronic mild inflammatory changes and occasional emphysema. No definite alterations in the respiratory epithelium or the peribronchial smooth musculature.	Lyon et al. (1970) B-12
Acrolein 0.51 (0.22)	77 ± 1°F, ~ 50%	Inhalation chamber	Squirrel monkeys (Saimiri sciurea)	18 M	18 M	90 d	90 d	No effect on behavior. 1 animal developed an eye infection in the 5th wk and died in the 6th wk. No effect on wt. gain or hematological values. Nonspecific inflammatory changes in the liver, lung, kidney, and heart.	Lyon et al. (1970) B-12

TABLE III-15. DOGS--REPEATED DOSE EXPERIMENTAL EXPOSURE TO ACROLEIN

Compound(s) and Concentration(s), mg/m³ (ppm)	Humidity/ Temperature	Mode of Exposure	Species/Strain/ Age/Weight	No. of Test Animals	No. of Controls	Duration and Frequency of Exposure	Total Length of Experiment	Effects	Reference and Rating
Acrolein 8.6 ± 1.9 (3.7 ± 0.8)	77 ± 1°F, ~ 50%	Inhalation chamber	Purebred beagle dogs	2 M	2 M	8 h/d, 5 d/wk, 6 wk	6 wk	During the 1st wk: salivated excessively, blinked frequently, kept eyes closed, and had difficulty breathing. Continued during 2nd wk, although less severe. Eye irritation continued the next 4 wk. Decreased rate of body wt. gain. No effect on hematological values, various liver and serum enzyme activities, or serum sulfobromophthalein retention. Nonspecific inflammatory changes in lung, liver, and kidney. Squamous metaplasia and basal cell hyperplasia of the trachea. Bronchopneumonia.	Lyon et al. (1970) B-12
Acrolein 4.2 (1.8)	77 ± 1°F, ~ 50%	Inhalation chamber	Purebred beagle dogs	2 M	2 M	90 d	90 d	Excessive salivation and ocular discharge. No effect on wt. gain or hematological values. Nonspecific inflammatory changes in the brain, heart, lung, liver, and kidney. Both animals showed confluent bronchopneumonia.	Lyon et al. (1970) B-12
Acrolein 2.3 (1.0)	77 ± 1°F, ~ 50%	Inhalation chamber	Purebred beagle dogs	2 M	2 M	90 d	90 d	Ocular and nasal discharge throughout exposure, decreasing in severity. No effect on wt. gain or hematological values. Focal inflammatory reactions involving lung, kidney, and liver. Bronchiolitis; and early bronchopneumonia in 1 dog.	Lyon et al. (1970) B-12

(continued)

TABLE III-15. (concluded)

Compound(s) and Concentration(s), mg/m³ (ppm)	Humidity/ Temperature	Mode of Exposure	Species/Strain/ Age/Weight	No. of Test Animals	No. of Controls	Duration and Frequency of Exposure	Total Length of Experiment	Effects	Reference and Rating
Acrolein 1.6 ± 0.2 (0.7 ± 0.1)	77 ± 1°F, ~ 50%	Inhalation chamber	Purebred beagle dogs	2 M	2 M	8 h/d, 5 d/wk, 6 wk	6 wk	No effect on behavior, body wt. gain, hematological values, various serum and liver enzyme activities, or serum sulfobromophthalein retention. Lungs showed mild chronic inflammatory changes and occasional emphysema. No definite alterations in the respiratory epithelium or the peribronchial smooth musculature.	Lyon et al. (1970) B-12
Acrolein 0.51 (0.22)	77 ± 1°F, ~ 50%	Inhalation chamber	Purebred beagle dogs	4 M	4 M	90 d	90 d	No effect on behavior, wt. gain, or hematological values. The lungs of 2/4 showed moderate emphysema, acute congestion, focal vacuolization of the bronchiolar epithelial cells with increased secretory activity, and, occasionally, some degree of bronchiolar constriction. Focal subcapsular hemorrhage in the spleens of the same 2. The other 2 showed hyperplasia of the thyroid. Nonspecific inflammatory changes in lung, liver, and kidney.	Lyon et al. (1970) B-12

TABLE III-16

SUMMARY OF ANIMAL INHALATION EXPOSURES TO ACROLEIN

Level	Time	Species	Effects
> 100-5,000	≤ 6 h	RAT GPG MUS CKN CAT	Deaths at higher levels and longer exposure times;strong respiratory irritation; decreased respiratory parameters; histopathological changes, particularly in the upper respiratory tract; some damage to other organs.
100	30 min, twice a day, 5 wk	MUS	Decreased pulmonary compliance; increased serum antitrypsin activity and lung total phospholipids.
93.2	15 min or 1 h	MUS	Respiratory difficulty; decreased body wt. 2 d later; recovery by 5 d.
72.2	6 h	MUS	No deaths.
50	1 min	RAT	Insignificant blood pressure changes; changes in heart rate.
46.6	15 min	RAT	40-50% decrease in respiration rate in 3 min.
34-46	4 h	CAT	Tearing, salivation, sneezing, nasal secretions, retching, dyspnea; recovered in several days.
39.6	60 min	GPG	Tracheotomy: no change in respiratory resistance, rate or minute volume. Inhalation: increased resistance; decreased rate; no change in compliance.
20-30	9 h 40 min	CAT	Salivation; sleepy; light retching; quiet.
28	4 h	RAT	Severe eye and respiratory tract irritation; dyspnea; anorexia; weakness; decreased lung and serum alkaline phosphatase (AP) activities.
28	~ 5 min	RBT	Decreased heart rate; increased arterial pressure; inhibited respiratory movement.
23-27	3.5 h	CAT	Tearing, salivation, sneezing, sleepy, mouth breathing.

TABLE III-16 (continued)

Level	Time	Species	Effects
25	1 min	RAT	Insignificant changes in blood pressure and heart rate.
21	~ 5 min	RBT	Slight increase in heart rate; no change in arterial pressure or respiratory movement.
18.6	4 h	RAT	Increased liver enzyme activities; slightly increased lung-to-body-wt. and liver-to-body wt. ratios.
14.9	4 h	RAT	Changes in liver enzyme activites; liver-to-body wt. ratio increased.
14	4 h	HAM	Cytopathological changes in the respiratory tract; no polymorphonuclear leukocyte recruitment.
< 14 on 593 mg/m^3 carbon particle	4 h	HAM	Leukocyte recruitment to tracheal and intrapulmonary airway epithelia.
11.4	6 h/d, 5 d/wk, 13 wk	HAM	Salivation; nasal discharge; decreased food intake and wt. gain; increased hematological values in females; changes in urinary values; increased lung-, heart-, and kidney-to-body wt. ratios; histopathological changes in lining of nasal cavity, and larynx of few females; hyper- and metaplasia in tracheal epithelium of some males and most females.
11.4	6 h/d, 5 d/wk, 13 wk	RAT	50% died in first 4 wk; decreased food intake and body wt. gain; no effect on hematological values and blood chemistry; changes in urinary values, increased relative wt. of lungs, heart, kidneys, and adrenals; histopathological changes in lining of nasal cavity and larynx; severe damage of trachea, lungs, and bronchi.

TABLE III-16 (continued)

Level	Time	Species	Effects
11.4	6 h/d, 5 d/wk, 13 wk	RBT	Sneezing and occasional breathing difficulty; decreased food intake and body wt. gain; increased relative wt. of lungs; no effect on hematology, blood chemistry, gross autopsy, histopathology of larynx; changes in lining of nasal cavity, trachea, bronchi, and lungs.
10.3	2-8 h	RAT	No changes in lung and liver alkaline phosphatase (AP) activity; changes in liver AP activity.
10	1 min	RAT	Insignificant changes in blood pressure and heart rate.
9.6	20 h	RAT	Increased liver- and lung-to-body wt. ratio, adrenals wt., liver AP activity; no change in lung and serum AP activity.
9.3	4 h/d, 5 d	RAT	Decreased liver-to-body wt. ratio; no change in lung, liver, and serum AP activity and lung and adrenal wts.
9.2	7 h/d, 5 d/wk, 52 wk	HAM	Slight decrease in body wt.; 20/36 died by 28 wk post-exposure; hematological parameters unchanged; slight to moderate epithelial metaplasia in nasal cavity; changes in other parts of respiratory tract; no tumors; possible slight co-carcinogenicity with benzo(a)pyrene.
9.1	4 h/d, 9 d	RAT	Decreased liver-to-body wt. ratio; no change in lung, liver, and serum AP activities and lung and adrenal wts.
8.6	8 h/d, 5 d/wk, 6 wk	MKY DOG GPG RAT	Mild irritation in MKY and DOG; 2/9 MKY died; decreased body wt. gain; no change in behavior (RAT and GPG), hematological values, or various enzyme activities; nonspecific inflammatory changes in lung, liver, kidney, brain (GPG only), and heart (GPG only); focal renal tubular calcification in MKY and RAT; squamous metaplasia and basal cell hyperplasia of the trachea in MKY and DOG; necrotizing bronchitis and bronchiolitis with squamous metaplasia of the lungs in MKY; bronchopneumonia in DOG.

TABLE III-16 (continued)

Level	Time	Species	Effects
4.9	41 h	RAT	Increased liver-to-body wt. ratio, adrenal wt., liver AP activity; no change in lung and serum AP activity and lung wt.
4.7	up to 91 d	RAT	Decreased wt. gain and vanillylmandelic acid levels; slight changes in ventilatory resistance; no change in hematological value; loss of bronchial cilia during first 5 wk; perivascular edema during days 35-90.
2.3-4.7 plus prior bacterial and viral exposure	4 or 24 h	MUS	Mild discomfort; significant decrease in pulmonary bactericidal activity by 24 h, varying with type of bacteria.
4.2	90 d	GPG RAT DOG MKY	Salivation and ocular discharge in DOG and MKY; no effect on wt. gain (except RAT, which decreased) or hematological values; nonspecific inflammatory changes in brain, heart, lungs, liver, and kidneys; confluent bronchopneumonia in DOG; squamous metaplasia of the trachea in MKY.
4.0	10 min	MUS	50-62% decrease in respiratory rate.
3.3	6 h/d, 5 d/wk, 13 wk	RBT HAM RAT	Restless; decreased food intake and body wt. gain in RAT and RBT; no effect on hematological values, blood chemistry, urinalysis, organ-to-body wt. ratios, gross autopsy, or histopathology of the larynx, trachea, bronchi, lungs, and, in RBT only, nasal cavity; minor inflammation of HAM nasal cavity; squamous metaplasia and neutrophilic infiltration of the mucosa of the RAT nasal cavity.
2.3	up to 91 d	RAT	Decreased wt. gain and vanillylmandelic acid levels; no effect on hematological values or respiratory resistance; slight loss of bronchial ciliation on days 7-35; perivascular edema after 35 d.

TABLE III-16 (continued)

Level	Time	Species	Effects
2.3	90 d	DOG MKY GPG RAT	Decreasing ocular and nasal discharge in DOG and MKY; no effect on wt. gain (except RAT, which decreased) or hematological values; various degrees of pulmonary inflammation in DOG, GPG, and RAT; parasitic infection in MKY; occasional, slight liver damage in DOG and GPG; kidney inflammation in DOG.
2.3	81 h	RAT	No effect on liver-to-body-wt. ratio, adrenal and lung wt., and liver, lung, and serum AP activity.
2.3	2 h	GPG	Significantly increased respiratory resistance and rate and decreased tidal volume.
1.6	8 h/d, 5 d/wk, 6 wk	RAT GPG MKY DOG	No effect on behavior, body wt. gain, hematological values, various enzyme activities; mild chronic lung inflammation; occasional emphysema; no definite alteration of respiratory epithelia or the peribronchial smooth musculature.
1.52	24 d	RAT	Progressive deterioration of general condition; 7/10 died; changes in magnitude and latent period of conditioned motor response; decreased blood cholinesterase activity and increased leukocytes, returning to normal by 20 d post-exposure; lung inflammation; myocardium and liver changes.
1.23-1.47	6 mo	RAT	Decreased body wt.; alveolar damage; liver cell damage; no effect on alveolar macrophages, spleen, kidney, stomach, or heart.
1.4	2 h	GPG	Increased expiratory flow resistance and tidal volume and decreased respiration rate, max. change in 30-60 min.
1.24-1.31	10-180 d	RAT	Decreased number of alveolar macrophages on days 10-26; no effect on relative no. of cells, viability, and physiological activity; no effect on days 60-180.

TABLE III-16 (continued)

Level	Time	Species	Effects
1.24-1.31	15, 18 21, 26 32, 60, 63, or 77 d	RAT	Increased lung-to-body-wt. ratio only on day 77; no effect on various enzyme activities; decreased body wt. during 21-d exposure; no effect on no. of pregnant rats or no. and avg. wt. of fetuses for 26-d exposure; significantly increased mortality when a high bacterial dose followed an 18-d exposure, but not after a 63-d exposure.
0.93	6 h/d, 5 d/wk, 13 wk	RBT HAM	No effect on behavior, growth, food intake, hematological values, blood chemistry, urinalysis, organ-to-body wt. ratios, gross autopsy, or histopathology of the respiratory tract.
0.9	2 h	GPG	Significantly increased total respiratory resistance; decreased respiratory rate.
0.74	61 d	RAT	General state and wt. affected by 6th wk in healthy rats and by 5th wk in rats with experimentally induced silicosis; changes in chronaxy of antagonistic muscles in both groups.
0.51	90 d	DOG GPG MKY RAT	No effect on behavior, wt. gain, hematological values, gross autopsy (RAT, MKY, GPG, DOG, with exceptions noted below). MKY & GPG & DOG - nonspecific inflammatory changes in liver, lung, kidney, and heart. DOG - Some of the following: emphysema, lung congestion, some bronchiolar constriction, hyperplasia of the thyroid, focal subcapsular hemorrhage of the spleen.
0.51	61 d	RAT	No change in behavior or general condition; lost wt.; loss of conditioned reflexes after 10 d; disturbance of spatial relationships; decreased urine coproporphyrin levels and blood cholinesterase activity; recovery post-exposure; some histopathological changes in the bronchi.

TABLE III-16 (concluded)

Level	Time	Species	Effects
0.47	2 h	GPG	Slight increase in total respiratory flow resistance; slight decrease in respiratory rate and minute volume.
0.15	61 d	RAT	No change in behavior, general condition, wt., magnitude or latent period of conditioned motor reflexes, urine coproporphyrin levels, or blood cholinesterase activity; no appreciable changes found on autopsy.
0.14	61 d	RAT	Changes in chronaxy of antagonistic muscles in healthy rats and rats with silicosis.
0.03	61 d	RAT	No change in a variety of biological, biochemical, and physiological tests in healthy rats or rats with silicosis.

SECTION IV

EXPERIMENTAL HUMAN INHALATION EXPOSURES

Table IV-1 describes acute laboratory human exposures to acrolein. Table S-4 in the Summary condenses all the information regarding experimental human exposure. The American Conference of Government Industrial Hygienists gives 0.25 mg/m^3 as the time-weighted-average threshold limit value (TLV) and 0.8 mg/m^3 as the short-term-exposure limit (ACGIH, 1980). The 8-h TLV promulgated by the Occupational Safety and Health Administration is also 0.25 mg/m^3 (0.1 ppm) (SRC, 1979).

TABLE IV-1. HUMANS - ACUTE EXPERIMENTAL INHALATION EXPOSURE TO ACROLEIN

Compound(s) and Concentration(s) in mg/m^3 (ppm)	Mode of Exposure	No. of Test Subjects	No. of Controls	Duration and Frequency of Exposure	Total Length of Experiment	Effects	Reference and Rating
Acrolein 2.33-46.6 (1-20) Levels in the whole diesel engine exhaust gas tested	Subject's face held 1 m downstream from exhaust pipe			2-3 eye blinks, without breathing		When 1-5 ppm acrolein was present, little to moderate eye irritation was reported. 5-10 ppm caused moderate to strong and intolerable eye irritation. > 10 ppm was intolerable and caused strong to extremely strong irritation.	Iwai et al. (1976) B-7
Acrolein 12.8 (5.5) CH_3Cl 1,138? (544.5?) (Exposure atmosphere made from a 1% acrolein-methyl chloride mixture)	Chamber	5		1 min	1 min	5 s: slight odor of acrolein, moderate nasal and eye irritation. 20 s: painful eye and nasal irritation. 1 min: marked lacrimation, practically intolerable.	Yant et al. (1930) C-10
Acrolein 4.7-5.4 (2.0-2.3)	Loose-fitting face mask with respirator, so only the eyes were exposed	26 M 10 F	Served as own controls	5 min	5 min	On a scale from 0 (none) to 2 (severe), the avg. maximum eye irritation was 1.476. The values for carbon-filtered air were 0.088-0.361.	Darley et al. (1960) C-10

(continued)

TABLE IV-1. (continued)

Compound(s) and Concentration(s) in mg/m^3 (ppm)	Mode of Exposure	No. of Test Subjects	No. of Controls	Duration and Frequency of Exposure	Total Length of Experiment	Effects	Reference and Rating
Acrolein 2.3-4.6 (1-2)	Eye exposure only through snugly fitting goggles	13-20 M+F for a total of 23 exposures	Served as own controls during the 5 min before exposure	5 min, repeated 3 times at unknown intervals		20 of 23 exposures (87%) caused eye irritation (medium or severe).	Stephens et al. (1961) B-8
Acrolein 4.19 (1.8) CH_3Cl 372? (178?) (Exposure atmosphere made from a 1% acrolein-methyl chloride mixture)	Chamber	6		4 min	4 min	30 s: odor of acrolein. 1 min: slight eye irritation and no nasal irritation. 2 min: slight nasal and distinct eye irritation. 3 min: slight nasal and distinct eye irritation, with lacrimation. 4 min: profuse lacrimation, practically intolerable.	Yant et al. (1930) C-10
Acrolein 4	Inhalation		10			Acute irritation of the conjunctiva and nasal mucosa. Painful sensations in the nasopharyngeal region.	Plotnikova (1960) A-9
Acrolein 3.0-3.7 (1.3-1.6)	Loose-fitting face mask with respirator, so only the eyes were exposed	26 M 10 F	Served as own controls	5 min	5 min	On a scale of 0 (none) to 2 (severe), the avg. maximum eye irritation was 1.182. The values for carbon-filtered air were 0.088-0.361.	Darley et al. (1960) C-10

(continued)

TABLE IV-1. (continued)

Compound(s) and Concentration(s) in mg/m^3 (ppm)	Mode of Exposure	No. of Test Subjects	No. of Controls	Duration and Frequency of Exposure	Total Length of Experiment	Effects	Reference and Rating
Acrolein 3.5 (1.5)	Eye irritation booths attached to a chamber	Not given	Not given	5 min	5 min	Caused medium to severe eye irritation.	Schuck and Renzetti (1960) C-8 Schuck and Doyle (1959) C-8
Acrolein 2.80 (1.22)	Inhalation chamber	12 M, 18-45-y-old; all exposed simultaneously	Controls used; no. not given	5 min	Not given	Extremely irritating to all exposed mucous membranes. Lacrimation occurred within 5 s. Exposure for more than 5 min would have been extremely distressing.	Sim and Pattle (1957) B-9
Acrolein 2.33 (1) CH_3Cl 207? (99?) (Exposure atmosphere made from a 1% acrolein-methyl chloride mixture)	Chamber	7		5 min	5 min	1 min: slight nasal irritation. 2 min: slight nasal and eye irritation. 3 min: slight nasal and moderate eye irritation. 4 min: slight nasal and moderate eye irritation with lacrimation. 5 min: moderate nasal irritation and practically intolerable eye irritation with lacrimation.	Yant et al. (1930) C-10
Acrolein 2.3 (1)	Eye exposure only, through snugly fitting goggles	13-20 M+F for a total of 17 exposures	Served as own controls for the 5 min before exposure	5 min, repeated twice at an unknown interval		14 of 17 exposures (82%) caused eye irritation (medium or severe).	Stephens et al. (1961) B-8

(continued)

TABLE IV-'. (continued)

Compound(s) and Concentration(s) in mg/m^3 (ppm)	Mode of Exposure	No. of Test Subjects	No. of Controls	Duration and Frequency of Exposure	Total Length of Experiment	Effects	Reference and Rating
Acrolein 2.3 (1.0)	Injecting sample into nostril by a syringe	4-6				Odor threshold	Cormack et al. (1974) A-8
Acrolein 2	Inhalation					Sharp changes in the amplitude of respiratory movements as measures by a pneumograph, and a slight increase in respiratory frequency.	Plotnikova (1960) A-9
Acrolein 2		3, with odor thresholds of 0.8-0.9 mg/m^3	Served as own controls	5 min, during min 10-15 of the expt.	90 min	A sharp, unpleasant odor. Decreased eye sensitivity to light during exposure, followed by slow recovery. Near normal, fresh air values by 90 min. Changes in eye sensitivity to light may register functional changes in the brain.	Plotnikova (1960) A-9
Acrolein 1.75-2.0	Inhalation	3	Served as own controls	3 min	25 min	Shortened the optical chronaxy* (using the appearance of the phosphene** phenomenon) in 2/3 and prolonged it in 1. Returned to normal in all cases in 3-6 min. The rheobase*** was unaffected.	Plotnikova (1960) A-9
Acrolein 1.88 (0.805)	Inhalation chamber	12 M, 18-45-y-old all exposed simultaneously	Controls used; no. not given	10 min	Not given	Extremely irritating to all exposed mucous membranes. Lacrimation occurred with 20 s. Exposure for the full 10 min was only just tolerable.	Sim and Pattle (1957) B-9

(continued)

* Optical chronaxy is the minimum time an electric current must flow at a voltage twice the rheobase*** to cause a muscle to contract.
** Phosphene is an objective visual sensation that appears with the eyes closed and in the absence of visual light.
*** The rheobase is the minimum potential of electric current necessary to produce stimulation.

TABLE IV-1. (continued)

Compound(s) and Concentration(s) in mg/m³ (ppm)	Mode of Exposure	No. of Test Subjects	No. of Controls	Duration and Frequency of Exposure	Total Length of Experiment	Effects	Reference and Rating
Acrolein 1.5	Inhalation					Slight changes in amplitude of respiratory movements, as measured by a pneumograph.	Plotnikova (1960) A-9
Acrolein 0.6-1.5	Inhalation	3	Served as own controls	3 min	25 min	No effect on the rheobase or optical chronaxy at 0.6, 1.0, or 1.5 mg/m³ in any of the subjects.	Plotnikova (1960) A-9
Acrolein 1.4 (0.6)	Climatic chamber	17 M 25 F	Served as own controls	7.5 min; 5 x 1.5-min exposures at 8-min intervals	39.5 min	Subjective air quality above that for intermittent exposure to lower levels and below that for continuous, rising exposure to 0.6 ppm. Desire to leave the room about equal to that for both intermittent and continuous exposures. Slight eye and nose irritation, a little above intermittent exposure to lower levels, but well below that of continuous, rising exposure to 0.6 ppm.	Weber-Tschopp et al. (1977) A-14

(continued)

TABLE IV-1. (continued)

Compound(s) and Concentration(s) in mg/m^3 (ppm)	Mode of Exposure	No. of Test Subjects	No. of Controls	Duration and Frequency of Exposure	Total Length of Experiment	Effects	Reference and Rating
Acrolein 0-1.4 (0-0.6) Level steadily increasing during the first 35 min, then constant	Climatic chamber	31 M 22 F; all were exposed, but only 34 used for blinking frequency and 19 for respiratory frequency measurements	Served as own controls	40 min	40 min	Continuously increasing annoyance (as measured by subjective judgment of air quality and the desire to leave the room) with increasing acrolein level. A significant difference from short, discontinuous exposures to similar levels only for 0.15 ppm (higher for noncontinuous), indicating some adaptation to acrolein at continuous exposure to lower levels, which disappears at higher levels. Eye irritation continuously increased from none to severe, and nose irritation from none to moderate. The level of irritation was always greater than that during short (~ 1.5 min), individual exposures to similar levels, the difference increasing with time and exposure levels. This indicates an increase in sensitivity of both organs during continuous exposure. Blinking frequency began increasing at 0.17 ppm, was significant at 0.26 ppm, and continued increasing. A significant decrease (~ 25%) in respiratory frequency by 0.6 ppm, with other changes such as irregularity in depth and elongated expiration.	Weber-Tschopp et al. (1977) A-14

(continued)

TABLE IV-1. (continued)

Compound(s) and Concentration(s) in mg/m^3 (ppm)	Mode of Exposure	No. of Test Subjects	No. of Controls	Duration and Frequency of Exposure	Total Length of Experiment	Effects	Reference and Rating
Acrolein 1.2 (0.5)	Eye exposure only, through snugly fitting goggles	13-20 M+F	Served as own controls, for the 5 min before exposure	5 or 12 min, each repeated 4 or 8 times, with various members of the group		For 12-min exposures, 30 of 33 exposures (91%) caused eye irritation (medium or severe). For 5-min dynamic exposures with 4 repetitions, 7 of 36 exposures (19%) caused eye irritation. For 5-min static exposures with 8 repetitions, 25 of 72 exposures (35%) caused eye irritation.	Stephens et al. (1961) B-8

(continued)

TABLE IV-1. (continued)

Compound(s) and Concentration(s) in mg/m^3 (ppm)	Mode of Exposure	No. of Test Subjects	No. of Controls	Duration and Frequency of Exposure	Total Length of Experiment	Effects	Reference and Rating
Acrolein 1.2 (0.5)	Eye exposure only	4 M 2 F	Served as own controls	5 min	24 h	pH of the tear fluid decreased in 3/6 and stayed the same in 3/6 (avg. ~ 7.1 before and ~ 6.9 after); tear volume increased in 3/6 and decreased in 3/6 (avg. ~ 6.5 µL/5 min before and ~ 7.5 after); lysozyme activity (volume/min) in the tear fluid increased in 3/6 and decreased in 3/6 (avg. showing an overall slight decrease); lysozyme activity (concentration) decreased slightly overall. 1-24 h after exposure: significant decrease in avg. pH of the tear fluid (avg. ~ 6.8) by 2 h, then increase to near normal value by 24 h; significant increases in avg. tear volume by 2 h (~ 11 µL/5 min) and 8 h (~ 13 µL/5 min), then decrease by 24 h but still above normal; avg. lysozyme activity (volume/min) increased at 2 and 5 h, was significantly increased at 8 h (~ 27 µg/min vs. ~ 18 µg/min), then slight decrease at 24 h though still above normal; avg. lysozyme concentration decreased for 8 h, then increased towards normal levels. Individual differences were seen at all times for all parameters.	Harada (1977) B-8

(continued)

TABLE IV-1. (continued)

Compound(s) and Concentration(s) in mg/m^3 (ppm)	Mode of Exposure	No. of Test Subjects	No. of Controls	Duration and Frequency of Exposure	Total Length of Experiment	Effects	Reference and Rating
Acrolein 1.05 (0.45)	Climatic chamber	17 M 25 F	Served as own controls	7.5 min; 5 x 1.5-min exposures at 8-min intervals	39.5 min	Subjective air quality and the desire to leave the room equal to that of intermittent exposure to lower levels and continuous, rising exposure to 0.45 ppm. Very slight eye and nose irritation, equal to that of intermittent, lower exposures and well below that of continuous, rising exposures to 0.45 ppm.	Weber-Tschopp et al. (1977) A-14
Acrolein 1	Inhalation	10				Slight irritation of the conjunctiva and a stinging sensation in the nose.	Plotnikova (1960) A-9
Acrolein 0.8-1.0	Inhalation					No effect on respiration frequency or amplitude (as measured by a pneumograph); although the substance was clearly perceived by the subjects.	Plotnikova (1960) A-9
Acrolein 0.8-0.83		3, with odor thresholds of 0.8-0.9 mg/m^3	Served as own controls	5 min, during min 10-15 of the expt.	90 min	Increased eye sensitivity to light during exposure, with recovery to normal, fresh air values by 60 min.	Plotnikova (1960) A-9
Acrolein 0.82 (0.35)	Eye exposure only	9 M, 20-23-y-old		2 min		Concentration at which 70% of the subjects sensed eye irritation.	Mizoguchi et al. (1972) A-6
Acrolein 0.8	Inhalation	10				Minimum odor perceived by 9/10.	Plotnikova (1960) A-9

(continued)

TABLE IV-1. (continued)

Compound(s) and Concentration(s) in mg/m³ (ppm)	Mode of Exposure	No. of Test Subjects	No. of Controls	Duration and Frequency of Exposure	Total Length of Experiment	Effects	Reference and Rating
Acrolein 0.7 (0.3)	Climatic chamber	21 M 25 F; ~ 31 used for blinking frequency and 16 for respiratory frequency measurements	Served as own controls	60 min	60 min	Subjective air quality decreased continuously for ~ 20 min, then increased slightly. Eye, nose, and throat irritation all increased for ~ 40 min, then leveled off, the relative irritation decreasing in the order of organs given. Increased blinking frequency, correlated with eye irritation. Significant decrease (~ 20%) in respiratory frequency by 40 min, remaining near that level to the end. Occasional irregularities in respiratory depth and holding of breath.	Weber-Tschopp et al. (1977) A-14
Acrolein 0.7 (0.3)	Climatic chamber	17 M 25 F	Served as own controls	7.5 min; 5 x 1.5-min exposures at 8-min intervals	39.5 min	Subjective air quality and the desire to leave the room slightly above values for intermittent exposure to lower levels and above those for continuous, rising exposure to 0.3 ppm. Almost no eye or nose irritation, equal to that at lower intermittent exposure levels and well below that during continuous, rising exposure to 0.3 ppm.	Weber-Tschopp et al. (1977) A-14
Acrolein 0.6-0.65		3, with odor thresholds of 0.8-0.9 mg/m³	Served as own controls	10 min, during min 10-15 and min 45-50 of the expt.	90 min, with a 10-min pre-exposure period	Eye sensitivity to light increased sharply during both exposures, and decreased sharply at the end of each exposure. Response was the same as the control and fresh air values by 60 min. The threshold value for acrolein action on light sensitivity.	Plotnikova (1960) A-9

(continued)

TABLE IV-1. (continued)

Compound(s) and Concentration(s) in mg/m^3 (ppm)	Mode of Exposure	No. of Test Subjects	No. of Controls	Duration and Frequency of Exposure	Total Length of Experiment	Effects	Reference and Rating
Acrolein 0.5		3, with odor thresholds of 0.8-0.9 mg/m^3	Served as own controls	5 min, during min 10-15 of the expt.	90 min	Subthreshold level of acrolein action on eye sensitivity to light.	Plotnikova (1960) A-9
Acrolein 0.49 (0.21)	Odor test room	4 trained odor analysts	Served as own controls			Lowest concentration at which all the subjects positively recognized the odor.	Leonardos et al. (1969) B-13
Acrolein 0.35 (0.15)	Climatic chamber	17 M 25 F	Served as own controls	7.5 min; 5 x 1.5-min exposure at 8-min intervals	39.5 min	Increased annoyance (as measured by subjective judgment of air quality and desire to leave the the room) compared to controls and those exposed continuously to $\leq$ 0.15 ppm. Almost no eye and nose irritation, below that for continuous, rising exposure to 0.15 ppm.	Weber-Tschopp et al. (1977) A-14
Acrolein 0.33 (0.14)	Eye exposure only	9 M, 20-23-y-old		2 min		Concentration at which 30% of the subjects sensed eye irritation.	Hizoguchi et al. (1972) A-6
Acrolein 0.23 (0.1)	Odor room, 8.9 m^3	4-6		The minimum time required to make an assessment		Odor threshold; level at which 50% of the panelists detected the odor.	Cormack et al. (1974) A-8

(continued)

TABLE IV-1. (concluded)

Compound(s) and Concentration(s) in mg/m^3 (ppm)	Mode of Exposure	No. of Test Subjects	No. of Controls	Duration and Frequency of Exposure	Total Length of Experiment	Effects	Reference and Rating
Acrolein 0.14						Odor threshold.	VanGemert and Nettenbreijer (1977) A--
Acrolein 0.14 (0.06)	Loose-fitting face mask with respirator, so only the eyes were exposed	26 M 10 F	Served as own controls	5 min	5 min	On a scale of 0 (none) to 2 (severe), the avg. maximum degree of eye irritation was 0.471. The values for carbon-filtered air were 0.088-0.361.	Darley et al. (1960) C-10
Acrolein 0.078		27, "practically healthy," 18-35-y-old				Threshold concentration for odor detection for the most sensitive people.	Ubaidullaev and Abramova (1976) A-6
Acrolein 0.07		"Volunteers"		"Short-term"		Odor threshold for sensitive subjects.	Sinkuvene (1970) B-8
Acrolein 0.05						Threshold concentration affecting electrical activity of the cortex of the brain.	Ubaidullaev and Abramova (1976) A-6; Sinkuvene (1970) B-8
Acrolein 0.03						Subthreshold level for electrical activity of the cortex of the human brain.	Ubaidullaev and Abramova (1976) A-6

SECTION V

OTHER HUMAN EXPOSURES

Only two occupational exposure studies were found. These are described in Table V-1. Neither is useful due to the presence of confounding factors, poor or no air measurements, and no controls.

No epidemiological studies of acrolein exposure were found.

Two case reports of accidental exposures to acrolein are described in Table V-2. Because of the unknown and probably high levels of acrolein involved, these are of little use in helping to determine a range of concern for automotive emission of acrolein.

TABLE V-1. STUDIES OF OCCUPATIONAL EXPOSURE TO ACROLEIN

Compounds and Concentrations in mg/m^3 (ppm)	Population Group: Description	Population Group: Exposed	Population Group: Control	Effects	Remarks	Reference and Rating
HCHO and acrolein from smoke developed from cutting and sealing polyethylene bags at high temperatures (presumably > 240°C). No concentrations determined.	Four workers in two 8-h shifts operated the thermocutting and sealing apparatus. One worker nearby, sitting in the draft, was less exposed. Sometimes the remaining workers also were exposed.	> 5 F	--	The 4 engaged in cutting and sealing complained of symptoms from skin and from the mucous membranes of the eyes and respiratory tract: burning in the eyes, dryness and irritation of the facial and neck skin and less so of the forearms. Heavy smoke exposure produced skin eruptions, especially around the eyes. Drowsiness and headache were noted at the end of the day. The worker sitting nearby complained of same symptoms, but lesser degree. All 5 workers gave a positive response to a patch test with a 40% aqueous HCHO solution. When the other workers in the room were annoyed by the smoke, the cutting operation was shut down. The only ventilation was via the windows, which they were reluctant to open in cold weather.	Essentially case reports of exposure to small amounts of smoke from from cutting polyethylene bags. No measurements and no follow-up after changes in the ventilation system.	Hovding (1969) D-4
Acrolein (< 0.014 - < 0.04) HCHO (0.015 - 0.07) CO (< 1 - 15) NO_x (0.03 - 0.26) SO_2 (< 0.01) Total particulates 0.09 - 0.26	Workers in the Run and Service Building of the Union Pacific Railroad in Pocatello, Idaho. Air measurements done on April 9-10, 1972. Medical evaluation done on April 19-20, 1972.	90 M in this building; 27 M in other areas (exposure levels of these men not given)	Results of a study of 10,000 industrial workers used for comparison to the spirometry test results	Workers and some of the men taking air samples complained of burning eyes. 31/114 were classified as having symptoms of bronchitis, as determined by questionnaire. 12/114 had abnormal spirograms (compared to expected 7.2), not statistically significant. No pneumoconiotic lesions were identified on chest x-ray. The conclusion was that excessive chronic respiratory disease probably did not exist.	Primarily a study of the occurrence of the gases, not a health effects survey. For the purposes of this study, the effect of acrolein is confounded by the presence of several other gases.	Apol (1973) D-5

TABLE V-2. HUMANS--STUDIES OF ACCIDENTAL EXPOSURES TO ACROLEIN

Compounds and Concentrations in mg/m^3	Duration of Exposure	Accident Description	No. of Victims	Description	Reference and Rating
Acrolein not given	~ 2 h	Inhaled the smoke from an overheated frier.	2 M (4.5- and 2-y-old)	The 2-y-old was found dead. On hospitalization 6 h later, the 4.5-y-old was somnolent and lightly cyanotic, with moderate respiratory difficulty. Oxygen therapy was applied 24 h after exposure, respiratory functions deteriorated rapidly and the trachea was obstructed by a firm, elastic substance. Death occurred quickly, due to asphyxiation. On autopsy: total obstruction of the trachea and bronchi by a thick mucus secretion, massive cellular desquamation of the bronchial lining, and multiple pulmonary infarcts.	Gosselin et al. (1979) C-5
Acrolein not given (probably high)	Not given (probably very short)	Worker in a chemical factory. A rupture sprayed acrolein in his face.	1 M, 39-y-old	Immediately felt a burning in his face and eyelids. 20 h later, presented subacute pulmonary syndrome with marked dyspnea, thoracic constriction, cough with frothy sputum, and cyanosis. On hospitalization: pale, cyanotic, edema of the eyelids, sweating, intense dyspnea, very fast respiration, cough with light red sputum, and pulmonary edema. Treated with oxygen, antibiotics, and cortisone. Left the hospital after 9 d, with a moderate cough and light dyspnea. 2 mo later: moderate tracheal edema and some blockage of the bronchial tube. 18 mo later: general state good, some dyspnea on exertion, slight opacities in the chest x-rays, and slightly increased residual volume (respiratory) at rest. Eventually, the subject presented signs of chronic broncho-pneumopathy, with chronic bronchitis and emphysema.	Champeix et al. (1966) C-8

ANNOTATED BIBLIOGRAPHY

6-046* Adamovich, G. G., O. V. Filippov, T N. Mikhailova, and Y. T. Kozlova. 1977. Immunobiological Activity of Workers in Relation to Length of Employment and Profession Under the Combined Effect of Chlorobenzene, Acetone, Acrolein, and Glass-Fiber Dust. Gigien. Aspekty Okhrany Zdorov'ya Naseleniya. 1977:107-108 (Russ).

D--.** This is a very brief discussion of the work described in Lychagin et al. (1976).

6-047 Aerts, C., A. B. Tonnel, N. Dutriez, and C. Voisin. 1979. In Vitro Sensitivity of Alveolar Macrophages to Gaseous Tobacco Smoke Components. Colloq. - Inst. Natl. Sante Rech. Med. 84 (Lavage Broncho Alveolaire Homme):177-185 (Fre).

D-7. The acrolein data are the same as those given in Voisin et al. (1979) [6-096] and Voisin et al. (1980) [6-099]. Studies were also done with cigarette smoke which contained 0-0.1 mg acrolein/unknown vol. Toxicity of the smoke appeared to be due to NO_2, not acrolein.

6-123 AIHA, American Industrial Hygiene Association. 1963. Hygienic Guide Series; Acrolein. American Industrial Hygiene Association, Akron, Ohio. 2 pp.

C--. Brief review. The ACGIH recommends an 8-h maximum atmospheric concentration of 0.5 ppm. However, it is suggested that this may be too high by a fivefold factor.

6-001 Albin, T. B. 1962. Handling and Toxicology. In: Acrolein, C. W. Smith, ed. John Wiley and Sons, Inc., New York, New York. pp. 234-239.

C--. Good brief review for handling and personal safety, less so for toxicology.

5-022 Altshuller, A. P. 1978. Assessment of the Contribution of Chemical Species to the Eye Irritation Potential of Photochemical Smog. J. Air Pollut. Control Assoc. 28(6):594-598.

D-8. A review and discussion of the results of several studies on atmospheric samples or irradiated auto exhaust and hydrocarbon-nitrogen oxide mixtures. The eye irritation on a moderately smoggy day may be due 40% to HCHO and 25% to acrolein. Atmospheric samples collected in California contained 30-66 ppb HCHO and 6-7 ppb acrolein.

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* Numbers in the left margin are MRI acquisition numbers.
** MRI rating system is described on pages 17-18.

6-126 Amdur, M. O. 1980. Air Pollutants. In: Toxicology, The Basic Science of Poisons. 2nd ed. L. J. Casarett and J.Doull, Eds. Macmillan Publishing Co., Inc., New York, New York. Chapter 24, pp. 608-631.

C--. Brief review.

6-116 Apol, A. G. 1973. Health Hazard Evaluation/Toxicity Determination. Report 72-32-42; Union Pacific Railroad, Pocatello, Idaho. PB-229 161, National Technical Information Service, U.S. Department of Cmmerce, Springfield, VA. 23 pp.

D--. 117 workers were exposed to acrolein (0.014-0.04 ppm), HCHO (0.015-0.07 ppm), CO (< 1-15 ppm), NO_x (0.03-0.26 ppm), SO_2 (< 0.01 ppm), and particulates (0.09-0.26 mg/m^3). No excess of chronic respiratory disease. Eye irritation and headaches reported.

6-003 Aretinskii, B. V., S. V. Kazantseva, L. G. Fed'kina, Yu. A. Potoskuev, N. V. Bochenina, L. E. Stepanova, A. N. Dudyreva, I. M. Il'ina, and F. N. Gofina. 1971. Development of Silicosis under the Effect of Quartz Dust and Diesel Exhaust Fumes on an Organism. Tr. Tsentr. Nauchno-Issled. Proektn.-Konstr. Inst. Profil. Pnevmokoniozov. Tekh. Bezop. Issue 5:100-110 (Russ).

D--. A more intense development of silicosis was observed in rats that received 75 mg of quartz-containing dust once intratracheally and then were subjected daily for 6 h for 90 d to poisoning by diesel exhaust fumes (N oxides, 32-35 mg/m^3; acrolein, 0.95-1.4 mg/m^3).

5-191 Battista, S.P., and C. J. Kensler. 1970. Mucus Production and Ciliary Transport Activity. In Vivo Studies Using the Chicken. Arch. Environ. Health 20:326-338.

C-9. In vivo, a dose of 35-40 µg acrolein/40-mL puff (875-1,000 mg/m^3) for 8 puffs inhibited ciliary transport activity to 50% that of the tracheas of control hens. A log concentration-percent inhibition curve for acrolein is given.

6-005 Beckner, J. S., P. M. Hudgins, and J. L. Egle, Jr. 1974. Effects of Acetaldehyde, Propionaldehyde, Formaldehyde, and Acrolein on Contractility, ^{14}C-Norepinephrine and $^{45}Calcium$ Binding in Isolated Smooth Muscle. Res. Commun. Chem. Pathol. Pharmacol. 9(3):471-488.

D-16. Good , well-done pharmacology. Mechanisms of structural congeners on isolated rat vas deferens and rabbit aorta (smooth muscle). Does not help define inhalation exposure levels. 0.01 M HCHO and 0.001 M acrolein gave similar responses.

6-140 Bittersohl, G. 1974. Epidemiologic Investigations on Cancer Incidence in Workers Contacted by Aldol and Other Aliphatic Aldehydes. Arch. Geschwulstforsch. 43(1):172-176 (Ger).

D--. MAC's for acrolein are 0.25 mg/m^3 in the DDR, BRD, and USA and 0.7 mg/m^3 in the UdSSR.

6-006 Bouley, G. 1973. Effects of Atmospheric Pollutants on Health. Econ. Med. Anim. 14(2):97-100 (Fre).

C-4. The exposure of animals (unclear whether rats or mice, possibly both) to 0.5 ppm acrolein for varying lengths of time, from 1 mo to the entire life span, caused decreasd growth and decreased levels of liver redox coenzymes. No experimental details are given. Perhaps the same study reported in detail in Bouley et al. (1975) [6-008].

6-008 Bouley, G., A. Dubreuil, J. Godin, and C. Boudene. 1975. Toxic Effects on Rats of a Continuous Inhalation of a Slight Dose of Acrolein. Eur. J. Toxicol. Environ. Hyg. 8(5):291-297.

B-10. Exposure of rats to 0.55 ppm acrolein for up to 77 d caused decreased weight gain and food consumption as long as the exposure lasted. Hepatic and respiratory effects and an increase in susceptibility to respiratory infection occurred during the first ~ 3 weeks, then disappeared spontaneously although exposure continued.

6-007 Bouley, G., A. Dubreuil, J. Godin, M. Boisset, and C. Boudene. 1976. Phenomena of Adaptation in Rats Continuously Exposed to Low Concentrations of Acrolein. Ann. Occup. Hyg. 19(1):27-32.

B-10. An English translation of Bouley et al. (1975) [6-008].

6-119 Bridges, R. B., J. H. Kraal, L. J. T. Huang, and M. B. Chancellor. 1977. Effects of Cigarette Smoke Components on In Vitro Chemotaxis of Human Polymorphonuclear Leukocytes. Infection and Immunity 16(1):240-248.

C-11. The concentrations required in the liquid phase to reduce the chemotactic responsiveness of PMN cultures by 50% of control levels were:

cyanide	3.5 mM
sulfide	6.5 mM
acrolein	15 μM

6-134 Brooks, S. M., C. F. Reinhardt, F. N. Marzulli, R. C. Graham, and J. Bender. 1981. Health Effects of Some Other Aldehydes. In: Formaldehyde and Other Aldehydes. Committee on Aldehydes, National Research Council. National Academy Press. Washington, D.C. pp. 221-255.

C--. Includes a review of acrolein toxicity through several routes of exposure, including inhalation.

5-129 Carpenter, C. P., H. F. Smyth, and U. C. Pozzani. 1949. The Assay of Acute Vapor Toxicity and the Grading and Interpretation of Results on 96 Chemical Compounds. J. Ind. Hyg. Toxicol. 31:343-346.

D-5. Study to develop a toxicity screening method. 250 ppm HCHO or 8 ppm acrolein for 4 h killed 2-4 of 6 albino rats.

6-120 Carson, S., R. Goldhamer, and M. S. Weinberg. 1966. Characterization of Physical, Chemical, and Biological Properties of Mucus in the Intact Animal. Ann. N. Y. Acad. Sci. 130:935-943.

D--. Primarily a discussion of the effects of cigarette smoke. Included a statement that acrolein was most effective of several respiratory irritants in reducing mucus flow rates in cats after short-term inhalation exposures.

6-010 Catilina, P., L. Thieblot, and J. Champeix. 1966a. A Trial Treatment of Respiratory Diseases Induced Experimentally in the Rat by Inhalation of Acrolein. Arch. Mal. Prof. 27(10):797-803 (Fre).

C-6. All of the 5 rats exposed to 1,000 mg acrolein/m^3 for 10 min died within 4 d of acute asphyxia. On autopsy, blocking of the airways by membranes, pulmonary hemorrhages and infarctions, and obstruction of the fine bronchioles by mucus and pus were noted. When followed by repeated treatment with Dexamethasone and/or Oxolamine, mortality was reduced.

6-095 Catilina, P., L. Thieblot, and J. Champeix. 1966b. Experimental Respiratory Lesions in Rats from Acrolein Inhalatin. Arch. Mal. Prof. 27(12):857-867 (Fre).

C-10. Detailed description of the anatomical and histopathological changes in rats following 10-min exposures to high levels of acrolein ($\geq$ 600 mg/m^3). A more complete report of the experiments and results also given in Catilina et al. (1970) [6-009].

6-009 Catilina, P., J. Champeix, and G. Andraud. 1970. Experimental Study of Pulmonary Toxic Substances. The Example of Acrolein. Poumon Coeur 26(8):867-876 (Fre).

C-9. A detailed description of the pathological changes in rats exposed to high levels of acrolein for 10 min: persistent bradypnea; destruction of epithelia; intense edema of the trachea, glottis, and bronchi; and congestion, hemorrhage, and infarction in the lung. 800 mg/m^3 (LC_{65}) and 750 mg/m^3 (LC_{50}) were fatal in 4 or 6-8 d, respectively. 650-700 mg/m^3 caused more delayed death.

5-378 Chaigneau, M. 1980. Classification of Harmful Gases. Ann. Anesthesiol. Fr. 21(6):683-688 (Fre).

D--. Very brief reviews (with no references) of the toxicity of several gases, including HCHO. Acrolein is mentioned as being lethal in $\leq$ 10 min at 30-100 ppm.

6-113 Champeix, J., and P. Catilina. 1967. Acrolein Poisoning. Masson et Cie, Paris, France (Fre).

C--. Same animal experimental information given in Catilina et al. (1970) [6-009], Catalina et al. (1966a) [6-010], and Catilina et al. (1966b) [6-095]. Also includes reviews of properties, sources, analysis methods, prevention, therapy, and human exposure.

6-011 Champeix, J., L. Courtial, E. Perche, and P. Catalina. 1966. Acute Broncho-Pneumopathy from Acrolein Vapors. Arch. Mal. Prof. 27(10):794-796 (Fre).

C-8. Case history of a man accidentally exposed to an unknown (probably high) level of acrolein for a short time. Within 20 h he was hospitalized with cough, frothy sputum, cyanosis, and a feeling of thoracic constriction. He developed extreme pallor and cyanosis, edema of the eyelids, intense dyspnea, and accelerated breathing. He was released 9 d later, with light cough and dyspnea. 18 mo later, dyspnea on exertion and slight opacities in the chest X-rays still existed.

5-220 Criteria for Community Air Quality Committee. 1968. Community Air Quality Guides. Aldehydes. Am. Ind. Hyg. Assoc. J. 28(5):505-512.

C--. The toxicology and ambient concentrations of specific aldehydes including HCHO and acrolein were reviewed. In automobile exhaust, ~ 70 mol-% of the carbonyl compounds, which are mainly aldehydes, is HCHO. Acrolein and acetaldehyde comprise 3-10 mol-%. Avg. U.S. urban air concentrations are 0.06 ppm HCHO (~ 0.09 mg/m^3) and 0.006 ppm acrolein (~ 0.014 mg/m^3). Recommended levels (causing no sensory irritation) are 0.1 ppm HCHO, 0.01 ppm acrolein, and 0.2 ppm total aldehyde as HCHO.

6-013 Dahlgren, S., and T. Dalhman. 1966. The Effect of Oxolamine Citrate on Experimentally Produced Inflammation in the Respiratory Organs. ACTA Pharmacol. Toxicol. 24(2-3):286-296.

D-9. Respiratory tract irritation in guinea pigs was induced by a 10-min inhalation of an aerosol of a 250 ppm acrolein solution. Those animals receiving only treatment with NaCl showed fairly severe macroscopic changes in the pulmonary parenchyma indicating inflammation. Treatment with anti-inflammatory drugs decreased the level of inflammation.

6-014 Dahlgren, S. E., and T. Dalhamn. 1972. Antiinflammatory Action of Phenyl-Methyl-Oxadiazole (PMO): An Experimental Study on the Guinea Pig Trachea. Acta Pharmacol. Toxicol. 31(3):193-202.

D-9. Tracheal inflammation of the acute desquamating type was induced in guinea pigs by a 5-min inhalation of an aerosol of a 5% acrolein solution. Immediate, continuing treatment with PMO (orally or intraperitoneally administered) for 72 h significantly reduced the inflammation.

6-012 Dalgren, S. E., H. Dalen, and T. Dalhamn. 1972. Ultrastructural Observations on Chemically Induced Inflammation in Guinea Pig Trachea. Virchows Arch. Abt. B Zellpathol. 11(3):211-223.

D-7. The tracheal epithelium of guinea pigs was examined by light and electron microscopy 72 h after exposure to a 5% acrolein aerosol for 5 min. A great variation in the degree of epithelial damage was seen. Damage included loss of cilia, thick layers of heterophil granulocytes, altered organelles, and cytoplasmic vacuoles.

5-228 Dalhamn, T., and A. Rosengren. 1971. Effect of Different Aldehydes on Tracheal Mucosa. Arch. Otolaryngol. 93(5):496-500.

C-5. A study of rabbit tracheal tissue showed that HCHO appeared to be the most ciliotoxic, followed by acetaldehyde and acrolein. The experiments largely confirmed the results of other authors. Acrolein was tested over the range of 31.2 to 247.8 mg/m^3, causing ciliostasis in ~ 36 and ~ 6 min, respectively.

6-111 Darley, E. F., J. T. Middleton, and M. S. Garber. 1960. Plant Damage and Eye Irritation from Ozone-Hydrocarbon Reactions. J. Agric. Food Chem. 8(6):483-485.

C-10. Exposure of only the eyes to 0.06-2.3 ppm acrolein for 5 min caused very slight to strong irritation.

5-230 Davis, T. R. A., S. P. Battista, and C. J. Kensler. 1965. Effect of Cigarette Smoke, Acrolein and Formaldehyde on Pulmonary Function. Fed. Proc. 24(2, Part I):518.

C-5. An abstract of work in Davis et al. (1964) [5-131]. Exposure of both tracheotomized and intact guinea pigs to 17 ppm acrolein or 50 ppm HCHO, with effect on lung function only in intact animals.

5-131 Davis, T. R. A., S. P. Battista, and C. J. Kensler. 1967. Mechanism of Respiratory Effects During Exposure of Guinea Pigs to Irritants. Arch. Environ. Health 15:412-419.

C-6. Exposure of guinea pigs to HCHO and acrolein using both tracheotomized and intact animals. Effect on lung function only in intact animals.

6-015 Denine, E. P. 1971. A Histologic Assessment of the Effects of Acrolein Inhalation on the Replacement of Mechanically Denuded Tracheal Epithelium. Ph.D. Dissertation. University Microfilms International, A Xerox Company, Ann Arbor, Michigan.

C-12. Exposure to 200 ppm acrolein for 5 min/d, up to 2-7 d, caused ciliary loss and an inflammatory response in intact chickens, and retarded cilia regeneration in chickens with mechanically denuded tracheas. Similar exposure to 50 ppm caused less severe changes in intact animals and had no effect on regeneration.

6-016 Denine, E. P., S. L. Robbins, and C. J. Kensler, 1971. The Effects of Acrolein Inhalation on the Tracheal Mucosa of the Chicken. Toxicol. Appl. Pharmacol. 19(2):416.

D-4. Whole chickens exposed to 50 or 200 ppm acrolein through an endotracheal cannula for 1-27 d (5 min/d) showed changes in the tracheal mucosa increasing with exposure time and concentration. Only an abstract of work, so few experimental details are given. High levels are studied.

6-132 ECAO, Environmental Criteria and Assessment Office. 1980. Ambient Water Quality Criteria for Acrolein. PB81-117277, National Technical Information Service, U.S. Department of Commerce, Springfield, VA. 99 pp.

C--. The review of the literature included inhalation exposures. Several new documents were acquired based on its bibliography.

5-005 Egle, J. L. 1972. Retention of Inhaled Formaldehyde, Propionaldehyde, and Acrolein in the Dog. Arch. Environ. Health 25:119-124.

D-9. Anesthetized dogs were exposed to 0.15-0.35 μg HCHO/mL or 0.4-0.6 μg acrolein/ml. Retention of HCHO in the total respiratory tract was nearly 100%; upper tract retention alone exceeded 95%. Retention of acrolein on the total respiratory tract was 81-84%, upper tract retention was 75-80%. Variations in concentration, ventilatory rate, or tidal volume had little effect on retention of the chemicals.

5-183 Egle, J. L., and P. M. Hudgins. 1974. Dose Dependent Sympathomimetic and Cardioinhibitory Effect of Acrolein and Formaldehyde in the Anesthetized Rat. Toxicol. Appl. Pharmacol. 28:358-366.

D-6. Primarily a study of i.v. exposure. Anesthetized rats were exposed by inhalation for 1 min to 0.01-5.00 μg acrolein/mL. As concentration increased a pressor effect of increasing magnitude was observed. Cardioinhibitory concentrations up to 2.50 and 5.00 μg/mL. HCHO concentrations up to 2.0 μg/mL did not produce any significant cardiovascular effects.

5-174 Fassett, D. W. 1963. Aldehydes and Acetals. In: Industrial Hygiene and Toxicology, 2nd revised ed. F. A. Patty, D. W. Fassett, and D. D. Irish, Eds. Interscience Publishers, New York, New York. Vol. 2, pp. 1959-1989.

C--. Contains little information specifically about acrolein. The 30-min LC_{50} for acrolein in rats was 130 ppm.

6-052 Feron, V. J., and A. Kruysse. 1977. Effects of Exposure to Acrolein Vapor in Hamsters Simultaneously Treated with Benzo(a)pyrene or Diethylnitrosamine. J. Toxicol. Environ. Health 3(3):379-394.

B-13. Exposure of hamsters to 4 ppm acrolein 7 h/d, 5 d/wk, for 52 wk caused slightly decreased body weights, increased nasal lesions, and no respiratory tract tumors. Co-exposure to benzo(a)pyrene caused slightly increased tumor incidence and to diethylnitrosamine caused no increase. A very good study, with good control groups. Numbers too small for use as a study on the carcinogenicity of acrolein.

6-053 Feron, V. J., A. Kruysse, H. P. Til, and H. R. Immel. 1978. Repeated Exposure to Acrolein Vapour: Subacute Studies in Hamsters, Rats and Rabbits. Toxicology 9(1-2):47-58.

B-13. A good study; rats, hamsters, and rabbits were exposed to 0, 0.4, 1.4, or 4.9 ppm acrolein for 6 h/d, 5 d/wk, for 13 wk. Irritation, decreased growth, and histopathological changes occurred in all species at the higher levels. At 0.4 ppm, rats showed abnormalities, but the other species seemed unaffected.

6-054 Fischer, T., A. Weber, and E. Grandjean. 1978. Air Pollution Due to Tobacco Smoke in Restaurants. Int. Arch. Occup. Environ. Health 41(4):267-280 (Ger).

D--. Levels of acrolein, CO, NO_2, and NO due to tobacco smoke were determined in the air of five restaurants. The acrolein values were 5 to 10 ppb. Because the threshold of irritation of acrolein is 100 ppb, it was not considered further in this study.

6-056 Gosselin, B., F. Wattel, C. Chopin, P. Degand, J. C. Fruchart, D. Van der Loo, and O. Crasquin. 1979. Case of Acute Acrolein Poisoning. Nouv. Presse Med. 8(30):2469-2472 (Fre).

C-5. A 4.5-y-old boy was hospitalized with acute respiratory failure following inhalation of the smoke (containing acrolein) from an overheated frier for 2 h. Asphyxia developed after 24 h. Tracheal destruction, massive cellular desquamation of the bronchial lining, and multiple pulmonary infarcts were found on autopsy. A 2-y-old boy died before treatment.

6-104 Guillerm, R., R. Badré, and B. Vignon. 1961. Inhibitory Effects of Tobacco Smoke on Epithelial Ciliary Activity and the Nature of the Responsible Components. Bull. Acad. Nat. Med. (Paris) 145 (20-21):416-423 (Fre).

C-7. 140 mg acrolein/m^3 (the level found in cigarette smoke) caused the complete inhibition of tracheal ciliary activity in 12 min. A mixture of acrolein (140 mg/m^3) and acetaldehyde (2,150 mg/m^3) caused cessation in 5.5 min, the same time as whole smoke.

6-018 Guillerm, R., A. Saindelle, P. Faltot, and J. Hee. 1967. Activity of Cigarette Smoke and Some of its Constituents on the Respiratory Resistance of Guinea Pigs. Arch. Int. Pharmacodyn. Ther. 167(1):101-114 (Fre).

D-9. The threshold level of acrolein causing increased ventilatory resistance in paralyzed and artificially ventilated guinea pigs was 19 ± 5 ppm. The level of acrolein measured in cigarette (Gauloise) smoke was ~ 200 ppm. A mixture of ethanol and acrolein at the levels found in the smoke caused the same respiratory changes as whole smoke.

6-105 Guillerm, R., J. Hee, M. Bourdin, H. Burnet, and G. Siou. 1974. Contribution to the Determination of the TLV Concentration of Acrolein. Cahiers INRS. No. 77:527-535 (Fre).

C-12. Groups of 50 rats were exposed to 1 or 2 ppm acrolein for 91 d. Changes in wt. gain, pulmonary resistance, hematology, pulmonary surfactant, urinary vanillylmandelic acid, and lung histology were reported for both levels.

6-019 Gumerov, N. K., and L. V. Virpsha. 1976. Physiological-Hygienic Appraisal of Working Conditions on Experimental Machines in the Construction of Main Pipelines. Gig. Tr. Okhr. Zdorov'ya Rab. Neft. Neftekhim. Prom-sti. 9:19-22 (Russ).

D--. Operators of pipe-laying machines were exposed to 368°C, 95 dB of noise, and cabin air concentrations of CO, gaseous hydrocarbons, and acrolein in concentrations of 3.8-70.6, 3.3-102.3, and 8.5-20.5 mg/m^3, respectively. Eight hours of work on this machine raised the operator's skin temperature significantly, prolonged the latent period of the visual motor reaction, and decreased the tolerance of static effort.

6-106 Gusev, M. I, A. I. Svechnikova, I. S. Dionov, M. D. Grebenskova, and A. I. Golovnia. 1966. Determination of the Daily Average Maximum Permissible Concentration of Acrolein in the Atmosphere. Hyg. Sanit. 31(1-3):8-13.

B-9. A nice study. Exposure of rats for 24 or 61 d showed 1.52 mg/m^3 to be a lethal dose (24 d), 0.51 mg/m^3, a toxic dose; and 0.15 mg/m^3, a safe dose. A wide range of physiological and biochemical parameters were considered. Recommends an avg. permissible concentration of 0.1 mg acrolein/m^3.

6-057 Harada, M. 1977. Photochemical Smog and Tear Fluid. Effects [of Smog] on pH, Volume, and Lysozyme Activity of Tear Fluid. Nippon Ganka Gakkai Zasshi 81(3):275-286 (Japan).

B-8. Much methods development. Includes a short section on 5-min exposure to 0.5 ppm acrolein and the subsequent analysis of tear fluid. Immediate changes occurred, but returned to near normal by 24 h. Eye irritation due to smog is measured, and the possible role of acrolein discussed.

6-020 Harke, H-P., A. Baars, B. Frahm, H. Peters, and C. Schultz. 1972. The Problems of Passive Smoking: Concentration of Smoke Constituents in the Air of Large and Small Rooms as a Function of Number of Cigarettes Smoked and Time. Int. Arch. Arbeitsmed. 29(4):323-339 (Ger).

C--. Concentrations of smoke constituents when 30 cigarettes were smoked in 13 min in a 38.2 m^3 room were 0.51 mg nicotine/m^3, 0.46 mg acrolein/m^3, 64 ppm CO, and 6.5 mg acetaldehyde/m^3. When 5 cigarettes were smoked in 13 min in a 38.2 m^3 room values were 0.06 mg nicotine/m^3, 0.07 mg acrolein/m^3, 11.5 ppm CO, and 1.3 mg acetaldehyde/m^3. When 150 cigarettes were smoked in 30 min in a 170 m^3 room: 0.69 mg nicotine/m^3, 0.38 mg acrolein/m^3, 53 ppm CO, and 4.2 mg acetaldehyde/m^3.

6-058 Haroz, R. K., and L. Mattenberger-Kreber. 1977. Effect of Cigarette Smoke on Macrophage Phagocytosis. In: Pulmonary Macrophage and Epithelial Cells. ERDA Symp. Ser. Vol. 43. CONF 760927, National Technical Information Service, U.S. Department of Commerce, Springfield, VA. pp. 36-57.

D-6. Method development paper. Only whole cigarette smoke tested. Various components of smoke and their levels in mg per cigarette were: HCN (272), NH_3 (24), H_2S (51), and acrolein (112). Acrolein did not appear to be implicated in the effect of whole smoke on alveolar macrophage function.

6-021 Hartzell, G. E., S. C. Packham, F. D. Hileman, S. C. Israel, M. L. Dickman, R. W. Mickelson, and R. C. Baldwin. 1976. Physiological and Behavioral Responses to Fire Combustion Products. In: Proc. 4th SPI Int. Cell. Plast. Conf. Nov 15-19, 1976. Technomic Publishing Co., Inc., Westport, Connecticut, pp. 264-270.

C-8. Various physiological and behavioral responses in rats during acute exposure to combinations of CO, CO_2, and acrolein. The addition of 20 ppm acrolein to 2,700 ppm CO appeared to increase the time to incapacitation. Minimal data given.

6-059 Hartzell, G., S. C. Packham, F. D. Hileman, S. C. Israel, M. L. Dickman, R. W. Mickelson, and R. C. Baldwin. 1977. Physiological and Behavioral Responses to Fire Combustion Products. In: Toxicity and the Products of Combustion; Fire Retard. Chem. Assoc. Annu. Meet, 4th, Washington, D.C., 1977. pp. 175-202.

C-8. Same information given in Hartzell et al. (1976) [6-021].

6-065 Heino, M., R. Ketola, P. Makela, R. Makinen, R. Niemela, J. Starck, and T. Partanen. 1978. Work Conditions and Health of Locomotive Engineers: I. Noise, Vibration, Thermal Climate, Diesel Exhaust Constituents, Ergonomics. Scand. J. Work Environ. Health 4(Suppl. 3):3-14.

D-7. Exposure data only, no health effects information. The mean levels in the atmosphere of roundhouses and locomotive cabs were: acrolein (0.03 and 0.01 ppm, respectively), HCHO (0.16 and 0.01), NO_x (0.13), and dust (1.99 and 0.38 mg/m^3).

6-022 Horton, A. D., and M. R. Guerin. 1974. Determination of Acetaldehydes and Acrolein in the Gas Phase of Cigarette Smoke Using Cryothermal Gas Chromatography. Tob. Sci. 176(4):45-48.

C--. An analytical methodology paper. Commercial and exptl. cigarettes (including a little cigar and a marijuana cigarette) contained 7-14 µg acrolein per puff.

5-140 Hovding, G. 1969. Occupational Dermatitis from Pyrolysis Products of Polythene. Acta Derm. Venereol. 49:147-149.

D-4. Case report of exposure to small amounts of smoke (presumably containing HCHO and acrolein) from cutting polyethylene bags. Symptoms of the skin and the mucous membranes of the eyes and upper respiratory tract were described. No measurements and no follow-up study after changes in the ventilation system.

6-066 IARC, International Agency for Research on Cancer. 1979. Monographs on the Evaluation of the Carcinogenic Risk of Chemicals to Humans, Vol. 19, Some Monomers, Plastics and Synthetic Elastomers, and Acrolein. World Health Organization, Geneva, Switzerland. pp. 479-494.

C--. Authoritative review of properties, uses, occurrence, toxicity, mutagenicity, and carcinogenicity of acrolein. States that the data are inadequate for an evaluation of carcinogenicity.

1-0172 ILO, International Labor Office. 1970. Permissible Levels of Toxic Substances in the Working Environment. Occupational Safety and Health Series 20, International Labor Office, Geneva, Switzerland. pp. 194-198.

C--. Maximum acceptable concentrations in Czechoslovakia:

	Normal MAC (mg/m^3)	Short, Single Exposure MAC (mg/m^3)
Acrolein	0.5	1.0
NH_3	40	80
HCHO	2	5
HCN	3	15
MeOH	100	500
H_2S	30	-

6-097 Iwai, T., K. Furui, A. Yoshida, and M. Tashiro. 1976. Measurement of Irritating Odor from Direct Injection Diesel Engines and Its Reduction Methods. In: 16th Int. Automob. Tech. Congr. Pap. No. 2-11. Tokyo, Japan. pp. 93-99.

B-7. Increasing acrolein (1-20 ppm) and aldehyde levels in diesel engine exhaust caused increasing eye and nose irritation in humans.

5-142 Iwanoff, N. 1911. On Some Aldehydes of Practical Importance. Arch. Hyg. 73:307-340 (Ger).

C-8. Acute exposure of cats to HCHO and acrolein. Study is of interest but of limited value because of the high dose levels used ($\geq$ 260 mg HCHO/m^3 and $\geq$ 25 mg acrolein/m^3).

6-067 Iwasaki, K. 1979. Combustion Gas Toxicity of Textiles. Sangyo Igaku 21(1):36-46 (Japan).

D--. Primarily a study of the combustion gases of different fabrics (gases contained trace to 500 ppm acrolein). Brief ($\leq$ 1 h) exposure to 40 ppm acrolein caused decreased wt. for several days following exposure.

6-068 Jakab, G. J. 1977. Adverse Effect of a Cigarette Smoke Component, Acrolein, on Pulmonary Antibacterial Defenses and on Viral-Bacterial Interactions in the Lung. Am. Rev. Respir. Dis. 115(1):33-38.

C-12. Exposure of mice to 1-2 ppm acrolein for 24 h, following brief bacterial exposure, suppressed pulmonary bactericidal mechanisms, the extent varying with the type of bacteria. The same exposure of mice already compromised by viral pneumonitis caused an even greater suppression of intrapulmonary bactericidal activity, proliferation of one bacteria occurring. A synergistic interaction between viral infection and acrolein exposure occurred. Results suggest a possible increase in frequency and severity of pulmonary infections following acrolein exposure.

6-024 Jermini, C., and A. Weber. 1975. Air Pollution by Cigarette Smoke. Soz.-Praeventivmed. 20(5):213 (Ger).

C--. Smoking 10 tobacco cigarettes in a 30 m^3 room produced the following concentrations of irritating substances: acrolein, 0.120 ppm; HCHO, 0.450 ppm; CO, 24 ppm; and NO, 0.678. The corresponding MAC's are 0.1, 2, 50, and 25 ppm, respectively.

5-208 Jermini, C., A. Weber, and E. Grandjean. 1976. Quantitative Determination of Various Gas-Phase Components of the Side-Stream Smoke of Cigarettes in the Room Air as a Contribution to the Problem of Passive-Smoking. Int. Arch. Occup. Environ. Health 36(3):169-181 (Ger).

D--. An unventilated 30 m^3 room in which 30 cigarettes were smoked contained 0.37 ppm acrolein. The unpolluted air in the room contained 0.036 ppm HCHO and 0.06 ppm HCHO after one cigarette was smoked. Other components were also measured.

5-010 Kane, L., and Y. Alarie. 1977. Sensory Irritation to Formaldehyde and Acrolein During Single and Repeated Exposures in Mice. Am. Ind. Hyg. Assoc. J. 38:509-522.

B-12. Mice exposed to low levels of HCHO and acrolein in single and repeated acute exposures with decreases in respiration rate. Kane and Alarie recommend a TLV of 0.03 to 0.3 ppm HCHO, and accept the TLV of 0.1 ppm acrolein.

6-069 Kane, L. E., and Y. Alarie. 1978. Evaluation of Sensory Irritation from Acrolein-Formaldehyde Mixtures. Am. Ind. Hyg. Assoc. J. 39(4):270-274.

B-10. A mathematical model applied to the data on the effects of acrolein and HCHO, alone and in 11 combinations, on the respiratory rate of mice indicates that competitive agonism exists between acrolein and HCHO when both are present.

6-070 Kane, L. E., and Y. Alarie. 1979. Interactions of Sulfur Dioxide and Acrolein as Sensory Irritants. Toxicol. Appl. Pharmacol. 48(2):305-316.

D-11. A study of mice exposed to mixtures of SO_2 (9-140 ppm) and acrolein (0.85-3.4 ppm). The results indicate the SO_2 can inactivate the effects of acrolein, and that a second sensory irritation occurs at the termination of exposure expressed as a post-exposure decrease in respiratory rate.

3-134 Kane, L. E., G. S. Barrow, and Y. Alarie. 1979. A Short-Term Test to Predict Acceptable Levels of Exposure to Airborne Sensory Irritants. Am. Ind. Hyg. Assoc. J. 40(3):207-229.

C-6. A discussion using the previous results of a short-term test with mice (effect on respiratory rate) to recommend exposure levels for many gases. Recommended highest concentrations for Air Quality Standards are: 0.002 ppm, acrolein; 0.3 ppm, NH_3; and 0.003 ppm HCHO. A TLV for acrolein in the range of 0.02-0.2 ppm is recommended.

6-026 Kantemirova, A. E. 1975. Illness with Temporary Work Disability in Workers Engaged in Acrolein and Methylmercaptopropionaldehyde (MMP) production. Tr. Volgogr. Gos. Med. Inst. 26(4):79-85 (Russ).

D--. Workers in the title industry were exposed to HCHO (0.05-8.1 mg/m^3), acrolein (0.1-8.2 mg/m^3), MeCHO (0.48-22 mg/m^3), methyl mercaptan (0.003-5.6 mg/m^3), and MMP (0.1-6.0 mg/m^3). Women working for < 1 or > 7 y had the most catarrhal diseases and the highest sick rates.

6-103 Kensler, C. J., and S. P. Battista. 1963. Components of Cigarette Smoke with Ciliary Depressant Activity. New Eng. J. Med. 269(22):1161-1166.

D-10. Ciliary transport rate of tracer particles in excised tracheal tissue was reduced 50% following exposure to 8 puffs containing 50 µg acrolein each. Requires major extrapolations to an in vivo exposure, but is a good mechanism for comparing compounds:

Gas	8 puff ED_{50} (µg/puff)
HCN	20
HCHO	6
NH_3	70
Acrolein	50
Acetaldehyde	1,300

5-367 Kettner, H. 1978. Indoor Contamination by Chemical Substances of Daily Use and Their Hygienic Significance. In: Org. Verunreinig. Umwelt: Erkennen, Bewerten, Vermidern, K. Aurand, V. Haesselbarth, E. Lahmann, G. Muller, and W. Neimitz, Eds. Erich Schmidt Verlag, Berlin, Germany. pp. 448-453 (Ger).

C--. Maximum allowable indoor air levels in the USSR:

Acrolein	0.1 mg/m^3
NH_3	0.2
HCN	0.002
HCHO	0.01
MeOH	0.5

5-072 Kilburn, K. H., and W. N. McKenzie. 1978. Leukocyte Recruitment to Airways by Aldehyde-Carbon Combinations that Mimic Cigarette Smoke. Lab. Invest. 38(2):134-142.

B-11. Exposure of hamsters to HCHO and acrolein, alone and with carbon particles. Effect only from the combination of two and very high levels of HCHO. Significant in relation to exhaust mixtures, especially diesel.

6-027 Kishi, M., S. Satoh, H. Tsuchiya, Y. Horiguchi, and Y. Wada. 1975. Effects of Inhalation of the Vapor from Heated Edible Oil on the Circulatory and Respiratory Systems in Rabbits. Shokuhin Eiseigaku Zasshi 16(5):318-323 (Japan).

C-8. Primarily a study of the effects of the vapors of heated oil on rabbits. Vapors contained up to 200 ppm acrolein, which apparently was the cause of the changes reported. Exposure to 9 or 12 ppm acrolein alone for ~ 5 min cause respiratory, heart rate, and blood pressure changes only at the higher level. Few experimental details of these studies given.

5-353 LaBelle, C. W., J. E. Long, and E. E. Christofano. 1955. Synergistic Effects of Aerosols. Particulates as Carriers of Toxic Vapors. A. M. A. Arch. Ind. Health 11:297-304.

C-6. Acute exposure of mice to HCHO and acrolein in combination with various aerosols. In general, aerosols increased the toxicity of HCHO and had no effect on acrolein.

6-071 Le Bouffant, L., J. C. Martin, H. Daniel, J. P. Henin, and C. Normand. 1980. Action of Intensive Cigarette Smoke Inhalations on the Rat Lung: Role of Particulate and Gaseous Cofactors. J. Natl. Cancer. Inst. 64(2):273-284.

D-7. A comparison of the effects of chronic exposure to high doses of cigarette smoke alone or in combination with coal dust or acrolein (level not given). The acrolein alone caused dyspnea and hypersecretion of mucus, with eventual adaptation, and had no effect on body wt.

6-072 Leffingwell, C. M., and R. B. Low. 1979. Cigarette Smoke Components and Alveolar Macrophage Protein Synthesis. Arch. Environ. Health 34(2):97-102.

D-11. A comparison of the effects of acrolein (in solution) and aqueous cigarette smoke extracts on amino acid incorporation into protein by rabbit pulmonary alveolar macrophages. At 6 μg/mL inhibition begain in ~ 1 h. The 60-min EC_{50} was 5.5 μg/mL, about four times the amount in the level of cigarette smoke (aqueous extract) causing 50% inhibition.

3-059 Leonardos, G., D. Kendall, and N. Barnard. 1969. Odor Threshold Determinations of 53 Odorant Chemicals. J. Air Pollut. Control Assoc. 19:91-95.

A-11. Definitive paper on the subject. Odor recognition thresholds were (ppm):

Acrolein	0.21
NH_3	46.8
HCHO	1.0
H_2S (from Na_2S)	0.0047
H_2S gas	0.00047
Methanol	100.0

6-075 Low, R. B., and C. A. Bulman. 1977. Substrate Transport by the Pulmonary Alveolar Macrophage: Effects of Smoke Components. Am. Rev. Respir. Dis. 116(3):423-432.

D-10. A mechanism study. The incubation of rabbit pulmonary alveolar macrophages with 0.6-60.0 µg acrolein/flask (vol. not given) for 1 h caused some inhibition of the transport of α-aminoisobutyrate, inhibition of cycloleucine transport at the longer exposure times and higher acrolein concentrations, and no effect on the transport of 3-O-methyl-D-glucose.

6-077 Low, E. S., R. B. Low, and G. M. Green. 1977. Correlated Effects of Cigarette Smoke Components on Alveolar Macrophage Adenosine Triphosphatase Activity and Phagocytosis. Am. Rev. Respir. Dis. 115(6 part 1):963-970.

D-10. A mechanism study. The incubation of rabbit lung alveolar macrophages with acrolein (3.45 µg/mL in solution) caused a 10% decrease in Ca-ATPase activity and a ~ 50% decrease in phagocytic ability and cell adhesion.

6-028 Lychagin, V. V., G. G. Adamovich, T. N. Mikhailova, Yu. G. Kozlova, Zh. V. Kinzhibalova, and O.V. Filippov. 1976. Assessment of Immunological Reactivity in Workers of Glass Insulation and Enamelling Departments in a Cable Plant. Gig. Tr. Prof. Zabol. No. 11:24-26 (Russ).

D--. In a cable plant, female workers were exposed in the insulation department to acrolein (0.1-1.0 mg/m^3), chlorobenzene, acetone, and glass fiber dust, and in the enameling department to acrolein (0.4-3.2 mg/m^3), chlorobenzene, and phenol. The respiratory, infectious, and immunological changes, seen more often in the insulation workers, were ascribed to the glass fiber dust and acetone.

6-029 Lyon, J. P., L. J. Jenkins, R. A. Jones, R. A. Coon, and J. Siegel. 1970. Repeated and Continuous Exposure of Laboratory Animals to Acrolein. Toxicol. Appl. Pharmacol. 17:726-732.

B-12. Good study of the exposure of rats, guinea pigs, dogs, and monkeys to 0.21-3.7 ppm for 8 h/d, 5 d/wk, for 6 wk, or continuously for 90 d. Only slight changes seen in most species at the lowest levels tested (0.22 and 0.7 ppm).

6-114 Masek, V. 1972. Aldehydes in the Air in Coal and Pitch Coking Plants. Staub-Reinhalt Luft. 32(8):335-336 (Ger).

D--. The maximum HCHO concentration measured was 1.972 mg/m^3, and the maximum acrolein level was 0.611 mg/m^3.

6-031 Meerson, E. A. 1975. Job Classification of Instrument Operators in Relation to Automatization. Tr. Volgogr. Gos. Med. Inst. 26(4):11-16 (Russ).

D--. The frequencies of heart contractions, gas exchange, and energy consumption were measured in four groups of plant personnel engaged in the production of S-containing compounds and exposed to acrolein, CH_3SH, CS_2, methylmercaptopropionaldehyde, methionine, Altax, Captax, thiuram E, and thiuram D. The groups were divided into extent of automation of their work, but concentrations of the compounds to which the groups were exposed were not given.

6-032 Mizoguchi, I., K. Makino, Y. Sato, M. Ohsawa, M. Chigusa, and H. Yagyu. 1972. Experimental Studies on Eye Irritation Due to Photochemical Smog. Tokyo Toritsu Eisei Kenkyusho Kenkyu Nempo 23:309-313 (Japan); English translation available from John Crerar Library, Chicago, Illinois. Order No. 73-14686-06F.

A-6. Good data for a threshold for eye irritation of 0.14-0.35 ppm acrolein.

6-108 Munsch, N., A. M. de Recondo, and C. Frayssinet. 1973. Effects of Acrolein on DNA Synthesis In Vitro. F. E. B. S. Letters 30(3):286-290.

D-9. Acrolein at high levels ($\geq$ 0.002 M) inhibited the action of partially purified regenerating rat liver DNA polymerase. Activation occurred at lower acrolein levels.

6-033 Murphy, S. D. 1965. Mechanism of the Effect of Acrolein on Rat Liver Enzymes. Toxicol. Appl. Pharmacol. 7(6):833-843.

D-9. Both the intraperitoneal injection (1-6 mg/kg) and the inhalation (8 ppm) of acrolein caused increased liver enzyme activity. For i.p. exposure, a dose-response relationship was found and the enzyme increases were much smaller when the animals were pretreated with protein synthesis inhibitors. An overly sophisticated study of local irritation after intraperitoneal injection.

6-117 Murphy, S. D., D. A. Klingshirn, and C. Ulrich. 1963. Respiratory Response of Guinea Pigs During Acrolein Inhalation and Its Modification by Drugs. J. Pharmacol. Exp. Ther. 141:79-83.

B-10. Guinea pigs exposed to 0.2, 0.4, 0.6, or 1.0 ppm acrolein for 2 h had increased total respiratory resistance and tidal volume and decreased respiratory rate, the degree of change increasing with increasing concentration. Treatment with one of several different drugs during acrolein exposure entirely reversed the increased respiratory resistance.

5-157 Murphy, S. D., H. V. Davis, and V. L. Zaratzian. 1964. Biochemical Effects in Rats from Irritating Air Contaminants. Toxicol. Appl. Pharmacol. 6:520-528.

C-8. Study of effect of acrolein (1-4 ppm, 20-81 h) and HCHO (18-h, 35 ppm) exposure on rat organ weight and alkaline phosphatase activity. The same values of concentration x time for acrolein had different effects, the continous exposures to the higher concentrations causing increased liver weight and enzyme activity.

6-124 Newsome, J. R., V. Norman, and V. L. Zaratzian. 1965. Vapor Phase Analysis of Cigarette Smoke. Tob. Sci. 9:102-110; or Tobacco 161(4):24-32.

D--. Levels in tobacco smoke (μg/40 mL puff):

	Unfiltered	Filtered
Methanol	13	10
HCHO	4.1	3.6
Acrolein	8.2	7.9
HCN	32	29
H_2S	3.4	3.1
NH_3	12	13

5-352 NRC. National Research Council. Panel on Vapor-Phase Organic Pollutants. 1976. Vapor-Phase Organic Pollutants. Volatile Hydrocarbons and Oxidation Products. Printing and Publishing Office, National Academy of Sciences, Washington, D.C. 411 pp.

C--. An authoritative, but brief, review of various aspects of acrolein and HCHO health effects literature is included in appropriate chapters of this book, which was used as a source of additional pertinent original papers.

6-073 Patel, J. M., J. C. Wood, and K. C. Leibman. 1980. The Biotransformation of Allyl Alcohol and Acrolein in Rat Liver and Lung Preparations. Drug Metab. Dispos. 8(5):305-308.

D-8. An *in vitro* study of the metabolism of acrolein by different lung and liver fractions, the mechanism and the end products (acrylic acid or glycidaldehyde) varying with the preparation.

6-074 Patel, J. M., E. Ortiz, and K. C. Leibman. 1981. Selective Inactivation of Rat Liver Cytochrome P-450 and of NADPH-cytochrome *c* Reductase by Acrolein. Personal Communication.

D--. The addition of acrolein to rat liver microsomal preparations caused the conversion of 50% of the cytochrome P-450 to cytochrome P-420, regardless of the acrolein concentration, and the total inactivation of NADPH-cytochrome *c* reductase activity in a concentration- and time-dependent manner.

1-0196 Pattle, R., and H. Collumbine. 1956. Toxicity of Some Atmospheric Pollutants. Br. Med. J. 2:913-916.

D-7. The exposure of mice, guinea pigs, and rabbits to 24.4 mg acrolein/m^3 for 6 h caused the death of ~ 50% in each species, due to severe tranceobronchitis with pulmonary edema, consolidation, congestion, and emphysema.

6-121 Philippin, C. L., E. Grandjean, and A. Gilgen. 1969. Physiological Effect of Acrolein on the Mouse. Praeventivmedizin 14(5):317-318 (Fre).

C-8. A study of 6-h exposure of mice to 31, 61, 80, or 119 ppm acrolein, and repeated exposure to 6, 15, 25, and 50 ppm. Deaths occurred only at $\geq$ 50 ppm exposures. Repeated exposure caused decreased body weight gain and swimming endurance, and lung pathology indicating inflammation.

6-034 Pinigin, M. A. 1972. New Approaches to the Solution of Urgent Problems in the Theory and Practice of Setting Hygienic Standards for Harmful Substances. PB-220-229T, National Technical Information Service, U.S. Department of Commerce, Springfield, VA. 30 pp.

D--. Data on animal mortality following acrolein inhalation were used as one example illustrating the author's views on setting hygienic standards.

6-088 Plotnikova, M. M. 1961. Basic Investigations for the Determinations of the Limit of Allowable Acrolein Concentration in Atmospheric Air. In: Limits of Allowable Concentrations of Atmospheric Pollutants No. 4. V. A. Ryazonov, Ed., B. S. Levine, translator. Office of Technical Services, U.S. Department of Commerce, Washington, D.C. pp. 59-71.

A-9. Several threshold levels were determined:

odor - 0.8 mg/m^3
optical chronaxy - 1.75 mg/m^3
respiratory amplitude and frequency - 1.5 mg/m^3
reflex effect on eye sensitivity to light - 0.6 mg/m^3

Author recommends a maximum single limit of allowable concentration in atmospheric air of 0.3 mg/m^3.

6-098 Potts, W. J., T. S. Lederer, and J. F. Quast. 1978. A Study of the Inhalation Toxicity of Smoke Produced Upon Pyrolysis and Combustion of Polyethylene Foams. Part I. Laboratory Studies. J. Combust. Toxicol. 5(4):408-433.

C-11. The smoke from the pyrolysis (nonflaming) of polyethylene-based materials was lethal to rats in the 48 h following a 30-min exposure. Gasping, strong eye irritation, salivation, and loss of coordination were observed during exposure. Authors believe the toxicity was due to the presence of acrolein (19-98 ppm from $\leq$ 1 g samples). This belief was strengthened by a study on pure acrolein giving a 30-min LC_{50} of 45-95 ppm.

6-110 Prentiss, A. 1937. Chemicals in War. McGraw Hill, New York, New York. pp. 139-140.

C--. A review with a nice summary of high dose effects:

7 mg/m^3 - severe irritation
50 mg/m^3 - intolerable
350 mg/m^3 - lethal in < 10 min

6-115 Protsenko, G. A., V. I. Danilov, A. N. Timchenko, A. V. Nenartovich, V. I. Trubilko, and V. A. Sauchenkov. 1973. Working Conditions When Metals to Which Primer Has Been Applied Are Welded Evaluated from the Health and Hygiene Aspect. Avtom. Svarka 26(2):65-68.

D--. Levels of many gases were determined under several different welding conditions: acrolein, 0.11-1.04 mg/m^3; and HCHO, 0.31-0.83 mg/m^3.

5-195 Renzetti, N., and R. Bryan. 1961. Atmospheric Sampling for Aldehydes and Eye Irritation in Los Angeles Smog. J. Air Pollut. Control Assoc. 11(9):421-424 and 427.

D-10. An attempt at correlating eye irritation and aldehyde levels in smog. Total aldehydes ranged from 0.02 to 0.40 ppm; HCHO from 0 to 0.13 ppm, and acrolein from 0.002 to 0.011 ppm. Good correlation was found for a log-probit relationship with total aldehydes, but the fit for HCHO was not as good.

6-082 Retnev, V. M., E. L. Sinitsyna, and V. N. Solov'ev. 1977. Physiological-Hygienic Labor Aspects of Repair-Setup Workers in the Machine Building Industry. Gig. Tr. Prof. Zabol. 5:46-47 (Russ).

D--. All exposures to acrolein (0-1.24 mg/m^3) were confounded by the presence of oil aerosols (0.5-39.5 mg/m^3) and CO (4.8-49.2 mg/m^3) and sometimes by SO_2 (0-10.3 mg/m^3) and alkaline aerosols ($\leq$ 0.5 mg/m^3).

6-083 Richter, M., and I. Erfurth. 1979. Gas Chromatographic Determination of Acrolein in its Original State in the Main Stream Smoke of Cigarettes. Description of an Analysis Method for Serial Determinations. Ber. Inst. Tabakforsch., Dresden 26:36-45 (Ger).

D--. Acrolein levels in six cigarette brands were 125.7-289.2 mμg/g tobacco solids.

6-036 Rickert, W. S., J. C. Robinson, and J. C. Young. 1980. Estimating the Hazards of Less Hazardous Cigarettes: 1. Tar, Nicotine, Carbon Monoxide, Acrolein, Hydrogen Cyanide, and Total Aldehyde Deliveries of Canadian Cigarettes. J. Toxicol. Environ. Health 6(2):351-366.

C--. Canadian cigarettes (102 brands purchased in March and April 1978) smoked usually to a 30-mm butt length contained 4-269 μg HCN/cigarette and 3-85 μg acrolein per cigarette. At 20 cigarettes per day, the average values per cigarette (168 and 65 μg, respectively) could contribute 4 and 68% of the exposure at the OSHA limits. It is not clear how the values of 432 ppm HCN and 78 ppm acrolein were calculated for deliveries per cigarette.

6-109 Roussel, A., G. Bouley, R. Roudier, A. Dubreuil, J. Godin, and C. Boudene. 1973. Prolonged Action of Low Doses of Acrolein in Rats. In: Proc. 3rd Int. Clean Air Cong., Dusseldorf, Germany. October 8-12, 1973. VDI-Verlag, Dusseldorf, Germany. pp. A17-A18 (Fre).

B-9. Rats exposed to ~ 0.6 ppm acrolein for 2-6 mo showed decreased food and water consumption, decreased lung and body weight, and some changes in the lungs and liver.

2-0051 Rylander, R. 1973. Toxicity of Cigarette Smoke Components. Free Lung Cell Response in Acute Exposures. Am. Rev. Resp. Dis. 108:1279-1282.

D-5. Guinea pigs were briefly exposed to cigarette smoke containing 7-74 μg acrolein/cigarette. The numbers of free macrophages and leukocytes in the lungs after exposure to the smoke from unfiltered cigarettes were inversely correlated to acrolein and other smoke components except NO.

5-264 Saindelle, A., F. Ruff, N. Flavian, and J. L. Parrot. 1968. Histamine Release by Short-Chain Aldehydes. C. R. Hebd. Seances Acad. Sci., Ser. D. 266(2):139-140.

D-7. 15,000 mL of gaseous acrolein (200 mL/m^3) was bubbled through 20 mL of liquid containing guinea pig lung fragments for 15 min. The amount of histamine released was 0-1.1 μg/g of tissue. This is less than that induced by a comparable volume of whole cigarette smoke.

5-161 Salem, H., and H. Cullumbine. 1960. Inhalation Toxicities of Some Aldehydes. Toxicol. Appl. Pharmacol. 2:183-187.

C-6. Exposure of mice, guinea pigs and rabbits to HCHO and acrolein in both vapor and aerosol form for up to 10 h. HCHO concentrations of 19-20 mg/m^3 caused few deaths during exposure, but a number of the animals died later. Acrolein at mean concentration of 4,624 to 5,225 mg/m^3 was lethal to all the animals in < 1 h. Mice were more susceptible to both HCHO and acrolein than other animals.

5-307 Schuck, E., and N. Renzetti. 1960. Eye Irritants Formed During Photooxidation of Hydrocarbons in the Presence of Oxides of Nitrogen. Air Pollut. Control Assoc. J. 10:389-392.

C-8. Moderate to severe eye irritation was caused by 5-min exposure to 1.5 ppm acrolein or 4 ppm HCHO. These two irritants accounted for most of the observed eye irritation caused by the products of the photooxidation of hydrocarbons with oxides of nitrogen. 3 ppm propionaldehyde and 10 ppm acetaldehyde caused no eye irritation.

6-038 Shmakov, A. A., G. A. Levit, A. N. Dudyrev, V. K. Agapova, V. S. Pridvizhkin, G. G. Nizhnikov, and B. V. Aretinskii. 1971. Sanitary and Hygienic Working Conditions after Introducing New Self-Propelled Equipment at the Mines of the Dzheskazgan Mining and Metallurgical Plant. Tr. Tsentr. Nauchno-Issled. Proektn.-Konstr. Inst. Profil. Pnevmokoniozov. Tek. Bezop. Issue 5:97-99 (Russ).

D--. Truck, bulldozer, and excavator drivers were exposed to ~ 14 mg acrolein/m^3 and ~ 10.4 mg NO_x/m^3, as well as noise, vibration, dust, and other fumes. Apparently no health evaluations were performed.

6-093 Silvestrini, B., and G. Maffii. 1959. Antitussive Activity Among Laboratory Animals and the Relation Between the Coughing Action and Other Pharmacological Properties. Farmaco (Sci. Ed.) 14(6):440-464 (Ital).

D--. A method of surveying the antitussive (anticough) activity of up to 16 substances by inducing coughing in rats, dogs, and guinea pigs with unknown (probably high) levels of NH_3, H_2SO_4, or acrolein.

6-094 Silvestrini, B., and C. Pozzatti. 1960. Antitussive Activity and Other Pharmacological Properties of Six Oxadiazoles. Arch. Int. Pharmacodyn. Ther. 129(3-4):249-263.

D-5. Acrolein was used at an unknown level as a standard irritant to cause coughing in guinea pigs. Subsequent treatment with different oxadiazoles resulted in different degrees of amelioration. Treatment of other problems, not caused by acrolein, was also tested.

1-0055 Sim, V. M., and R. F. Pattle. 1957. Effect of Possible Smog Irritants on Human Subjects. J. Am. Med. Assoc. 165:1908-1913.

B-9. A study of acute (< 30 min) human exposure to several compounds of interest. HCHO at 17.3 mg/m^3 was slightly irritating; acrolein at 1.88 or 2.80 mg/m^3 was extremely irritating; acetaldehyde at 240 mg/m^3 was mildly irritating; propionaldehyde at 324 mg/m^3 was mildly irritating. A more complex study of H_2SO_4 exposure was done.

6-040 Sinkuvene, D. S. 1970. Hygienic Assessment of Acrolein as an Air Pollutant. Hyg. Sanit. 35:325-329.

B-8. Thresholds for odor (0.07 mg/m^3) and cerebral cortex reflex activity (0.05 mg/m^3) are given. Exposure of rats, both sick and healthy, to 0.74, 0.14, or 0.03 mg/m^3 for 61 d caused changes in biological, biochemical, and physiological parameters at the two highest levels.

5-165 Skog, E. 1950. A Toxicological Investigation of Lower Aliphatic Aldehydes--I. Toxicity of Formaldehyde, Acetaldehyde, Propionaldehyde, and Butyraldehyde; As Well As of Acrolein and Crotonaldehyde. Acta Pharmacol. Toxicol. 6:299-318.

B-10. Acute exposure of rats to 600-1,700 mg HCHO/m^3 led to an LD_{50} of 1,000 mg/m^3. Rats exposed to 100-700 mg acrolein/m^3 had an LD_{50} of 300 mg/m^3. This is a solid acute, lethal dose study.

3-091 Smyth, H. 1956. Improved Communication--Hygienic Standards for Daily Inhalation. Am. Ind. Hyg. Assoc. Q. 17:129-185.

D--. Brief reviews of the toxicity of ~ 200 compounds, including acrolein, NH_3, HCN, H_2S, MeOH, HCHO, and H_2SO_4. Cites unpublished information that 8-h exposure to 8 ppm acrolein killed 1 of 6 rats.

6-133 Smyth, H. F., C. P. Carpenter, and C. S. Weil. 1951. Range-Finding Toxicity Data: List IV. AMA Arch. Ind. Hyg.Occup. Med. 4(2):119-122.

D--. Brief mention of acrolein with the same rat data as Smyth (1956).

6-089 Soriano, M. Experimental Asthma Produced by Acrolein. Arch. Med. Exp. 23(1):85-94 (Span).

C--. Guinea pigs exposed to 10% acrolein vapors suffered asthma characterized by bradypnea, spasmodic inspiration, and prolonged and difficult expiration rhonchus. Nasal and lacrimal secretion also occurred. Exposure for 1-2 min caused reversible symptoms, and normalization within 48 h. Exposure for 3-4 min caused irreversible asthma, and death due to acute emphysema and respiratory paralysis.

5-104 Sprince, H., C. M. Parker, and G. G. Smith. 1979. Comparison of Protection by L-Ascorbic Acid, L-Cysteine, and Adrenergic-Blocking Agents Against Acetaldehyde, Acrolein, and Formaldehyde Toxicity: Implications in Smoking. Agents Actions 9(4):407-414.

D-12. Rats were orally intubated with ~ 90% of the 24-h LD_{50} of HCHO or acrolein. Both groups gradually showed lethargy, tremors, respiratory distress, and death which suggested that the primary toxic effect, even through oral dosing, was on the repiratory system. Lung congestion and pulmonary edema at death are mentioned, but there is no description of histopathology or even gross necropsy.

6-118 SRC, Syracuse Research Corporation. 1979. Potential Occupational Hazards, Volume I, Single Chemicals; Acrolein. PB81-147951, National Technical Information Service, U.S. Department of Commerce, Springfield, VA. 23 pp.

A--. Extensive review.

5-306 Stephens, E., E. Darley, O. Taylor, and C. Scott. 1961. Photochemical Reaction Products in Air Pollution. Int. J. Air Water Pollut. 4(1-2):79-100.

B-8. Eye exposure only to 0.5-2 ppm acrolein for 5 or 12 min caused eye irritation in 19-91% of the people, the percentage increasing with increasing concentration, exposure time, or number of repetitions.

5-338 Stupfel, M. 1976. Recent Advances in Investigations of Toxicity of Automotive Exhaust. Environ. Health Perspect. 17:253-285.

D--. Summary of levels of various components of exhaust: HCHO in gasoline exhaust (10-300 ppm), HCHO in diesel exhaust (5-30 ppm), HCHO in urban polluted air (0.05-0.12 ppm), HCHO in tobacco smoke (120 ppm), acrolein in urban polluted air (0.01 ppm), acrolein in tobacco smoke (60 ppm), and HCN in tobacco smoke (300-1,500 ppm). Extensive review of epidemiology and human and animal experimental results of exposure to exhaust.

6-131 Tanimoto, M., and H. Uehara. 1975. Detection of Acrolein in Engine Exhaust with Microwave Cavity Spectrometer of Stark Voltage Sweep Type. Environ. Sci. Technol. 9(2):153-154.

D--. The exhaust of an automobile engine connected with a dynamometer contained ~ 5 ppm acrolein.

6-041 Ubaidullaev, R., and N. S. Abramova. 1976. Hygienic Standardization of the Combination of Acrolein, Acetone, and Phthalic Anhydride in the Air. Gig. Sanit. No. 10:6-10 (Russ).; English translation available from John Crerar Library, Chicago, Illinois. Order No. 80 13783-06J.

A-6. Primarily a study of mixtures of the three compounds, showing additive effects on odor perception and electrocortical activity. Acrolein alone had an odor threshold level of 0.078 mg/m^3 and an electrocortical activity threshold level of 0.05 mg/m^3.

6-091 Underhill, F. P. 1926. Chapter XIII. The Physiological Action of Miscellaneous Gases. In: The Medical Department of the United States Army in the World War. Vol. 14. Medical Aspects of Gas Warfare. U.S. Government Printing Office, Washington, D.C. pp. 407-420.

C--. Review of the toxicity of several compounds, including acrolein. Animal data were primarily about acute, lethal exposures. For human exposure:

~ 2.8 mg/m^3	odor threshold
7.7 mg/m^3	prominent eye and nose irritation
10.0 mg/m^3	pronounced lacrimation

3-094 U.S.S.R. State Committee of the Council of Ministers for Construction. 1972. Sanitary Norms for Industrial Enterprise Design. Publishing House of Literature on Construction, Moscow. 92 pp. (Russ).

C--. In the USSR, the MAC for acrolein in the workplace was 0.7 mg/m^3, and in populated places was 0.03 mg/m^3 (one-time and avg.).

5-413 Van Gemert, L. J., and A. H. Nettenbreijer. 1977. Compilation of Odor Threshold Values in Air and Water. National Institute for Water Supply. Leidschendam, The Netherlands, and Central Institute for Nutrition and Food Research, TNO, Zeist, The Netherlands. pp. 11, 23, 25, 33.

A--. Compilation of odor threshold values reported by different researchers, for many compounds, including:

ammonia	0.03 - 37 mg/m^3
HCN	< 1.1 - 6
H_2S	0.001 - 2
HCHO	0.033 - 2.2
Methanol	4.3 - 11,700
Acrolein	0.05 - 4.1

6-096 Voisin, C., C. Aerts, A. B. Tonnel, and N. Dutriez. 1979. Gaseous Aerocontaminants and Phagocytic Defense of the Respiratory Tract. Cytotoxicity of NO_2, of Ozone and Acrolein for Alveolar Macrophages in Gaseous Phase. Nouv. Presse Med. 8(25):2089-2094 (Fre).

C-9. Same data reported in Voisin et al. (1980) [6-099].

6-099 Voisin, C., F. Erba, N. Pommery-Dutriez, and C. Aerts. 1980. The Effects of Toxic Gases on Phagocytic Defenses of the Respiratory System; In Vitro Approach. Ann. Anesthesiol Fr. 21(6):639-643 (Fre).

C-9. Alveolar macrophage cultures from guinea pigs were exposed to gaseous acrolein (4-35 ppm) for 30 min. Decreased ATP levels were measured. Same data reported in Voisin et al. (1979) [6-096].

6-101 Von Oettingen, W. F. 1958. Poisoning; A Guide to Clinical Diagnosis and Treatment. 2nd ed., W. B. Saunders Co., Philadelphia, Pennsylvania. p. 216.

D--. Very brief review of symptoms, with no correlation to acrolein levels.

6-042 Watanabe, T., and D. M. Aviado. 1974. Functional and Biochemical Effects on the Lung Following Inhalation of Cigarette Smoke and Constituents: II. Skatole, Acrolein, and Acetaldehyde. Toxicol. Appl. Pharmacol. 30(2):201-209.

C-9. Exposure of mice to 100 mg acrolein/m^3 for 60 min/d for 5 wk or to 300 or 600 mg/m^3 for 5 min caused decreases in lung function values.

5-348 Weber, A., C. Jermini, and E. Grandjean. 1976a. Irritating Effects on Man of Air Pollution Due to Cigarette Smoke. Am. J. Public Health 66(7):672-676.

D-11. Exposure is confounded for the purposes of this report, but worth a mention as an interaction study with HCHO and acrolein as probably the primary irritants. The sidestream smoke from 30 cigarettes added to a 30 m^3 room for 26 min resulted in ~ 71 ppm CO, ~ 1.32 ppm HCHO, and ~0.30 ppm acrolein. The results of self-rated intensity of eye irritation paralleled the increases in irritants with time. Nose and throat irritation, respiratory and general complaints, and poor air quality judgments also increased with time, although weaker and less obviously paralleling irritant concentration. Nonsmokers were slightly more sensitive.

5-280 Weber, A., T. Fischer, E. Sancin, and E. Grandjean. 1976b. Air Pollution Due to Cigarette Smoke: Physiological and Irritating Effects. Soz.-Praeventivmed. 21(4):130-132 (Fre).

D-4. A group of 33 subjects was exposed to an increasing concentration of cigarette sidestream smoke for 28 min (containing 0.03-0.64 ppm HCHO, 1-43 ppm CO, 0.08-1.5 ppm NO, and 0-0.2 ppm acrolein). Eye irritation and subjective annoyance (the more sensitive criterion) increased with time, smokers and nonsmokers apparently equally sensitive. No significant differences in lung function were observed.

6-086 Weber-Tschopp, A., T. Fischer, R. Gierer, and E. Grandjean. 1977. Experimentally Induced Irritating Effects of Acrolein on Men. Int. Arch. Occup. Environ. Health 40(2):117-130 (Ger).

A-14. Short (1.5 min) exposures to 0.15, 0.30, 0.45, and 0.60 ppm acrolein, 35-min exposures to continuously rising (0-0.60 ppm) acrolein levels, and 60-min exposures to 0.30 ppm acrolein were studied. Significant changes were seen at the following concentrations:

Annoyance	0.09 ppm
Eye Irritation	0.09
Nose Irritation	0.15
Blinking Frequency	0.26
Respiratory Frequency	0.30
Throat Irritation	0.30

Exposures for the longer times generally caused more irritation, indicating lack of adjustment or desensitization to the irritating effects of acrolein.

6-112 Weissbecker, L., R. D. Carpenter, P. C. Luchsinger, and T. S. Osdene. 1969. In Vitro Alveolar Macrophage Viability; Effect of Gases. Arch. Environ. Health 18(5):756-759.

D-8. Exposure of a "hanging drop" cell mixture to 36-3,600 ppm acrolein, 373-3,700 ppm acetaldehyde, or 607-30,170 ppm HCN for 1 h caused no decrease in cell viability. The results section furnishes data indicating that these results are not properly reproducible, and therefore of little value.

6-044 Weissbecker, L., R. M. Creamer, and R. D. Carpenter. 1971. Cigarette Smoke and Tracheal Mucus Transport Rate. Isolation of Effect of Components of Smoke. Am. Rev. Resp. Dis. 104(2):182-187.

D-7. Anesthetized cats exposed to smoke from carbon-filtered cigarettes plus isoprene, NO, and acrolein had a 32% decrease in tracheal mucus flow. Little usefulness to this task because of the confounding presence of other gases and the lack of concentration information.

5-282 Wynder, E. L., D. A. Goodman, and D. Hoffman. 1965. Ciliatoxic Components in Cigarette Smoke. II. Carboxylic Acids and Aldehydes. Cancer 18(4):505-509.

C-8. The methods of this clam gill cilia study are not fully described. The lowest level of HCHO tested was 0.05% (500 ppm) and this produced almost immediate complete stasis of ciliary activity with eventual recovery. 0.1-1.0% (1,000-10,000 ppm) acrolein caused immediate and complete ciliastasis, while 0.05% (500 ppm) caused immediate lose of metachronic wave in the lateral cilia and partial stasis at ~ 1 min with no further effect.

6-092 Yant, W. P., H. H. Schrenk, F. A. Patty, and R. R. Sayers. 1930. Acrolein as a Warning Aent for Detecting Leakage of Methyl Chloride from Refrigerators. Report of Investigations 3027, Bureau of Mines, U.S. Department of Commerce. 11 pp.

C-10. The lowest concentration of acrolein tested (1 ppm) caused intolerable eye irritation in 5 min. A good time-to-effect study, but confounded by the presence of CH_3Cl (99 ppm).

5-121 Zitting, A., and H. Savolainen. 1979. Neurotoxic Effects of the Oxidative Thermal Degradation Products from Low Density Polyethylene. Fire Mater. 3(2):80-83.

C-10. Repeated exposure of rats to polyethylene combustion products containing 1.4 ppm HCHO, 0.5 ppm acrolein, ash, CO, and mixed aldehydes for 6 h/d, 5 d/wk for 2-5 wk led to undesirable neural effects.